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CANCER

ITS ORIGIN, ITS DEVELOPMENT AND ITS SELF-PERPETUATION

The Therapy of Operable and Inoperable Cancer in the Light of a Systemic Conception of Malignancy

A RESEARCH

BY Willy Meyer, M.D.

THIS WORK by the well-known American surgeon will be of interest to the entire medical profession. The book treats cancer as a systemic disease, with the malignant tumor as a late symptom. It emphasizes that both must be treated in order to effect a cure, and points the way toward definite immunization of patients against Cancer.

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Hope is held out for the favorable treatment of inoperable cancer on the basis of cited cases with actual results. Various methods, taken from every-day medical practice, are discussed, by means of which, under favorable conditions, a definite improvement may be expected.

PART I.

THE ORIGIN, THE DEVELOPMENT AND THE SELF-PERPETUATION OF CANCER

Cancer, the Product of Two Jointly Effective Chronic Irritations, One Systemic, One Local

PART II

THE THERAPY OF CANCER

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Non-Development of Eosinophilia in Pernicious Anemia Patients Treated With Desiccated Stomach*

By S. M. Goldhamer, M. D., *Ann Arbor, Michigan*

THE possibility of producing remissions in pernicious anemia under controlled conditions by the use of liver, liver extracts or stomach has opened the way for the careful study of the changes in the blood as the condition improves. The present paper deals with the changes in the eosinophile content of the blood. Minot and Murphy[1] noted that after a liver diet the polymorphonuclear eosinophile leucocytes occasionally increased to 20% or more, the rise persisting for many weeks. Whitby[2] reported an eosinophilia in four patients treated with raw or cooked liver. He felt that there was a relationship between the reticulocyte reaction and the increase in number of eosinophiles. Smith and Whitby[3] reported a definite absolute increase in the number of eosinophiles in all instances, ranging as high as 61% in a case of Hodgkin's disease after the use of liver. Ordway and Gorham[4] also noted the eosinophilia after liver therapy, and report that accompanying the increase in the number of red blood cells, the white blood cell count rises, and the polymorphonuclear neutrophiles and eosinophiles appear in greater numbers. One case showed a rise to 25% after one month of liver diet. Watkins and Berglund[5] reported a relatively constant percentage of eosinophiles up to the 18th day and then a marked increase ranging from 2 to 48% after this. They attributed this to a systemic reaction following an overdose of liver. Meulengracht and Holm[6] reviewed the literature of the subject and reported their own experience. They divided their patients into 3 groups; those receiving raw liver, cooked liver, and liver extract.

They found that a typical pronounced eosinophilia appeared only in those patients receiving raw liver, and concluded that eosinophilia was not characteristic of pernicious anemia only, but appeared in other individuals after the administration of the same quantity of raw liver. The various authors considered, but ruled out, the possibility of parasitic infection from the use of uncooked food and attributed the eosinophilia to some substance in the liver. Brower in a discussion of a paper on the treatment of pernicious anemia by the use of desiccated stomach, at the 1930 convention of the

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American Medical Association at Detroit, reported a very high eosinophilia in a patient treated with dried stomach. In Levine and Ladd's[7] series of 143 patients with pernicious anemia, 54 showed 5% or more eosinophiles at some time during the course of their disease, some reaching 25 per cent. These patients were not treated with liver or stomach tissue.

In order to note whether an eosinophilia was in any way related to the active principle which stimulates blood maturation in pernicious anemia or to some other constituent of liver, and to see whether it was also present in stomach tissue, the blood of 30 patients with typical pernicious anemia, who were being treated with dried stomach, was studied daily. The stools were examined with care to eliminate the possibility of infestation with intestinal parasites.

DATA

It was found that no gross eosinophilia above 5% developed in any patient who did not have any eosinophilia at the start. Of 6 patients with eosinophilia at the beginning of the treatment 2 had asthma or hay fever; 1 came from a family in which near relatives had asthma; and 2 had skin lesions. In one patient with a high eosinophile percentage (8.5—13%) before treatment no cause could be found. The presence of eosinophilia in patients of this type is a noteworthy fact, as the polymorphonuclear neutrophiles and basophilic leucocytes are frequently relatively, and usually absolutely, decreased in number during the leucopenia of the relapse in pernicious anemia. The pernicious anemia process does not inhibit the development of eosinophiles.

The average eosinophile percentage during the first 30 days of treatment with desiccated stomach, including all cases (both those with a high eosinophile percentage and the others) did not exceed 3.2%. This mixed group did not produce an average eosinophilia above 4.5% during the period of 8 to 16 weeks after the beginning of treatment (37 observations). Excluding the patients with an initial eosinophilia (i. e. above 5%) the average maximum for the first 30 days of treatment was 2.2%, and in 32 observations on this group during the next six months the highest average was 2.7%.

Of all the patients not showing an initial eosinophilia, two developed 8% eosinophiles, one on the 12th day of therapy, and not thereafter; and the other on the 11th day only. One showed 25% eosinophiles on one occasion at the end of the second month of treatment. The data concerning the number of eosinophile cells were compared to the red blood cell counts, the reticulocyte percentage and number, the hemoglobin percentage, and the total white blood cell count, and no simple correlation was evident.

Summary and Conclusion

1. No constant eosinophilia develops after treatment of pernicious anemia patients with desiccated stomach tissue.

2. In patients with allergic phenomena (asthma, hay fever, skin lesions), fundamental changes associated with pernicious anemia do not prevent the development of the character-

istic eosinophilia commonly seen in these conditions.

3. Eosinophilia may be present in pernicious anemia in the absence of an evident cause, and this sign is not a differential feature in the diagnosis of uncomplicated pernicious anemia and infestation with intestinal parasites.

4. There is no correlation between the changes in percentage, or absolute number, of eosinophile cells and the red blood cell count, hemoglobin percentage, or numerical changes in the reticulocytes.

5. The eosinophile stimulating substance of raw liver is not the active hematopoietic principle.

6. The eosinophile count cannot be used as a standard or index of the potency of the active blood maturing principle in desiccated stomach or liver extract.

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The Inhibitory Action of Infection and Fever on the Hematopoietic Response in a Case of Pernicious Anemia*

By Kenneth C. Smithburn, M.D., and L. G. Zerfas, M.D., *Indianapolis*

In the study of more than 150 cases of primary and secondary anemia, it has been frequently observed that fevers and intoxications of various origins have apparently retarded, interrupted, or prevented the hematopoietic response during active treatment. Minot[1] has pointed out that the hematopoietic response in cases of pernicious anemia treated with liver extract may be slight or delayed in the presence of complications. Whipple and his associates[2] have observed that infections and intoxications may retard the increase in hemoglobin production in experimental anemias.

The following patient, who came under our observation, demonstrates in a striking manner the effect of infection and fever on the response of the blood forming organs.

Report of Case

History: L. I., a white female, aged 53 years, a housewife, was admitted to the Indianapolis City Hospital on April 1, 1930, complaining of weakness, numbness and tingling in the extremities, sore mouth and tongue, icterus, constipation, dyspnea and palpitation on exertion. She first became ill in 1928, with nausea, vomiting, and epigastric pain. She lost strength rapidly and noticed that her skin was yellow. Her appetite became very poor and the sense of taste was markedly impaired. This condition persisted with temporary periods of remission until September 1929, when she first noticed sensations of numbness and tingling in her fingers and toes; the weakness became more extreme, and was accompanied by dyspnea and palpitation on slight exertion. About this time, also, nocturia, with pain and burning near the termination of urination, began. The patient's memory for details became very poor; she was markedly depressed and discouraged on admission to the hospital. She stated that her diet had consisted of fruits and vegetables and that she did not care for meats. She had lost about fifty pounds in weight in two years.

The past history was entirely negative. She was married at twenty-one, but had no pregnancies. The climacteric occurred in 1927. The family history was irrelevant.

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Physical Examination:

The skin and conjunctivae were of a lemon yellow color and were quite pale. The lingual papillae were atrophic; there were numerous channels over the tongue. All the natural teeth were absent. There was a soft systolic murmur over the mitral area. The blood pressure was 120 systolic and 62 diastolic. The spleen was palpable 3 cm. below the costal margin. The reflexes were normal. Otherwise the physical findings were essentially negative.

Laboratory Examination:

The erythrocyte count was 1.76 million, the leukocyte count 4,600 per cubic millimeter of blood, the hemoglobin 31.2% (Newcomer), and the reticulocyte (young red blood cell) count 2.1% (36,960 per cubic millimeter). The stained blood smears revealed the presence of many macrocytes typical of those observed in pernicious anemia during relapse. The blood bilirubin was 0.66 milligram per 100 cubic centimeters, and the diazo test showed a delayed positive reaction. The blood Wassermann was negative. The gastric analysis showed an absence of free hydrochloric acid and blood. The urinalysis showed: specific gravity 1.017; reaction, alkaline; albumin, a trace; 20 pus cells per high power field, centrifuged; a few tract cells.

A diagnosis of pernicious anemia was made.

Clinical Course:

Treatment with Liver Extract No. 343 was started on April 4, 1930. The daily dose was that amount derived from 300 grams of fresh liver, and this dose was maintained throughout the period of treatment. On April 14, the reticulocyte count had increased to 15% (250,500) and there was corresponding clinical improvement. On the following day the patient complained of frequency, urgency, burning on urination, and pain over the urinary bladder. The temperature, which had been within normal limits, rose to 102°, and the urine was loaded with pus and bladder epithelial cells. The reticulocyte count decreased to 10.9% (191,750). On April 17 she had a severe chill lasting about one hour, followed by a sharp rise in temperature to 106°, accompanied by nausea and vomiting. There was severe pain and marked tenderness in the region of the left kidney; urinalysis showed many pus cells and bladder epithelial cells and a considerable amount of albumin. The total non-protein nitrogen of the blood and the phenolsulphonephthalein test were normal. Leukocyte count was 4,000. Supportive treatment was given, and elimination was aided by the usual means. The response of the blood was completely inhibited during this attack of pyelitis and cystitis.

Following this acute illness the patient improved steadily. The temperature reached normal on April 23, but rose temporarily to 103.6°, this time attended by much less severe constitutional symptoms, and returned to normal on April 26. The urinary findings improved gradually, and the temperature remained normal. When the acute infection had subsided, there was again a sharp rise in reticulocytes to a peak of 22.6% (620,760) on April 27. The hemoglobin and erythrocytes in-

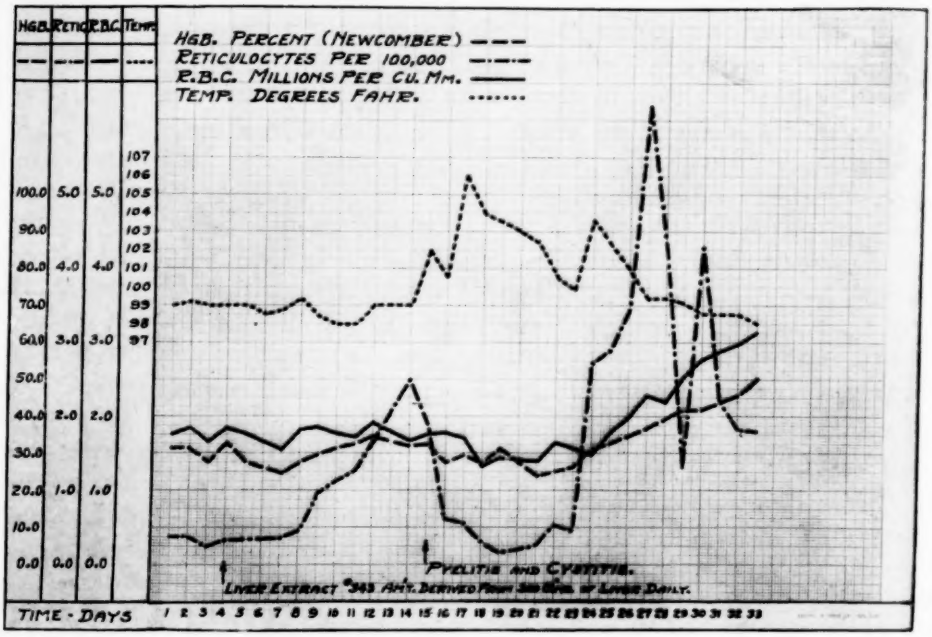

Chart I shows the levels of temperature, hemoglobin, erythrocytes, and reticulocytes before and during treatment, the inhibition of the hematopoietic response during the attack of pyelitis and cystitis, and recovery with a secondary reticulocyte response. The temperatures given are the highest recorded for the given day.

creased rapidly and there was marked improvement in the general condition of the patient. She was released from the hospital on May 6, 1930. At this time the red blood cell count was 3.12 million; the reticulocyte count was 5.8% (180,920); and the hemoglobin was 50%. Her appetite was good, the bowels regular, the color much improved, and she stated that she felt very well.

Zerfas[3] and others have shown that, in cases of pernicious anemia treated with liver extracts in adequate daily amounts, the average erythrocyte count at the end of one month's treatment is approximately 3.5 million, regardless of what low level the count may have reached before treatment was started. It is interesting to note that, in the case here reported, the red blood cell count at the end of one month's treatment was but 0.38 million below what would normally be expected, despite the fact that the response was suppressed for twelve days of this month.

Comment

In this case the control period of eleven days before the occurrence of fever seems to demonstrate clearly the inhibitory effect of fever or infection on the activity of the blood forming organs. Furthermore, the striking response occurring immediately follow-

ing subsidence of the fever and infection indicates clearly the advisability of continuing the daily administration of adequate amounts of liver extract in cases of pernicious anemia complicated by infection and fever.

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The Possible Significance of the Thymus Gland in the Syndrome of Hyperthyroidism*

By Harry M. Margolis, M. D., *Fellow In Medicine, The Mayo Foundation, Rochester, Minnesota*

IT IS significant that in reviewing the many reports concerning the relation of the thymus gland to hyperthyroidism one finds relatively few reports of careful histologic study of the affected glands. In most cases thymic hyperplasia is assumed merely on the basis of the increased weight of the thymus gland as compared with the weight of the normal gland. However, it is now well known, particularly as a result of the extensive and careful researches of Hammar[14], that one cannot draw accurate conclusions of the structure of the thymus gland, by a consideration merely of its weight. Histologic studies aiming to determine the structural characteristics and, to some extent, the quantitative relations of the various constituents of the thymic parenchyma and interstitium, are essential to determine the existence of pathologic hyperplasia or involution. Furthermore, such pathologic changes as are found in the various constituents of the thymus gland should be correlated with the salient clinical features in each case if the more obvious relationships between the thymus gland and the hyperthyroid syndrome are to be crystallized. For these reasons, a thorough investigation of the thymus gland in a series of cases of hyperthyroidism in which complete pathologic and clinical data were available was undertaken. The present report is concerned with the results of this investigation.

Review of Literature

Subsequent to the report of Moebius, more than a century ago, Markham described a typical case of exophthalmic goiter in which at necropsy the thymus gland was found remarkably enlarged. Mackenzie, in a review of thirty-six cases of exophthalmic goiter in which necropsy was performed, found the thymus gland considerably enlarged in a fair number of these. He said: "The most constant feature next to the enlarged thyroid is the presence in most cases of a persistent or enlarged thymus gland." He observed, however, in some cases that "although the gland was large, it showed the histological changes not of actively enlarged gland, but rather those of degeneration or some degree of fibrosis was present, but in other instances, it appeared like the gland of a child." Gierke claimed that enlarged

*Work done in the Section of Pathologic Anatomy, The Mayo Clinic. Submitted for publication May 1, 1930.

thymus glands are more common among patients dying soon after thyroidectomy than among the general group of thyrotoxic patients. Matti, reviewing the literature in a large number of cases of hyperthyroidism, also showed the common occurrence of thymic hyperplasia in patients dying after thyroidectomy. Similar reports on the frequent association of thymic hyperplasia and goiter have been made by Warthin, Crotti, Blackford and Freligh, Giordano, Potter and others. Potter regards the reaction of the thymus gland as a part of the lymphoid reaction characteristic of exophthalmic goiter. Klose and Warthin go so far as to assume that thymic hyperplasia is an invariable factor in the syndrome of hyperthyroidism. The absence of thymic hyperplasia in acute cases of long standing does not, according to Klose, preclude such a possibility. He suggests the possibility of secondary involution changes in the thymus gland incidental to the altered nutritional state of such patients and postulates the existence of aberrant thymus tissue that may be undergoing hyperplastic change.

Von Haberer has stressed the significance of partial thymectomy along with partial thyroidectomy in the treatment of hyperthyroidism. Although he often observed recurrence of symptoms of hyperthyroidism when thyroidectomy alone was performed, this did not occur when partial thymectomy was also done. Nordmann's experience indicated essentially the same thing. Crotti, in a series of 500 thyroidectomies for goiters of all types, in which he made a systematic search for thymic hyperplasia, had occasion to perform seventy-five thymectomies. Melchior, on the other hand, could not find any relation between the enlarged thymus gland frequently seen in hyperthyroidism and the course of the disease, or the postoperative results. He pointed out that recurrences following combined operations on the thymus and thyroid glands are just as frequent as when thyroidectomy alone is performed.

Among reports of histologic studies on the thymus gland in hyperthyroidism are those of Bayer who described marked broadening of the cortex and medulla with almost complete disappearance of the boundary between the cortex and medulla. Hassall's corpuscles were extraordinarily numerous and showed varying degrees of degeneration. Kocher indicated that histologically the thymus gland in cases of exophthalmic goiter is identical with that seen in juvenile hyperplasia of the thymus gland. Hammar's[13] studies showed that there was usually a marked increase in the cortical portion of the parenchyma, and a definite increase in the number of Hassall's corpuscles. Occasionally, he stated, the hyperplasia is confined to the medulla, and the quantitative relations between cortex and medulla are altered in favor of the medulla.

Results of Study

Eighty-five cases of hyperthyroidism in which complete necropsy data were available were studied. Fifty-five of these cases were diagnosed exophthalmic goiter, and thirty were diagnosed adenomatous goiter with hyperthyroidism. In each case the

clinical data left no doubt of the diagnosis and in most cases the clinical diagnosis was confirmed by the pathologic condition of the thyroid gland either at the time of operation or at necropsy. In certain cases in which undoubted clinical evidence of hyperthyroidism was present, stained sections revealed little evidence of hyperplasia in the thyroid gland. This was more often true of hyperfunctioning adenomatous goiter than of exophthalmic goiter. The clinical criteria on which were based the differentiation of exophthalmic goiter and hyperfunctioning adenomatous goiter were those established largely through the work of Mayo and Plummer. It may be noted that in nearly all cases in which exophthalmic goiter was diagnosed clinically some degree of diffuse parenchymatous hyperplasia and hypertrophy of the epithelium of the thyroid gland was found pathologically, whereas in cases diagnosed clinically adenomatous goiter with hyperthyroidism extra adenomatous hyperplasia of the thyroid epithelium was rarely encountered. In several cases of frank exophthalmic goiter adenomas were also present in the thyroid gland, but they were thought not to influence appreciably the production of the hyperthyroidism.

In all but eight of the fifty-five cases of exophthalmic goiter, some degree of hyperplasia of the thymic parenchyma was noted (table 1). In these eight cases there was either marked involution, or the entire thymic parenchyma had become replaced by fibro-areolar connective tissue which was entirely devoid of thymic cells or contained only scattered small thymic cells. It is notable that among the forty-seven cases in which there was thymic hyperplasia the gross weight of the thymus gland had increased in only twenty-eight. In the other nineteen cases the size of the thymus gland was not remarkable and the existing hyperplasia could not be detected without histologic study. On the other hand, of the eight cases in which striking involution was evidenced histologically, there was a definite increase in the weight of the thymus gland in four cases. Indeed, in one of these cases the gross weight of the thymus gland was 148 gm., the largest weight recorded for any of the thymus glands in the entire series. However, histologic studies of numerous sections from this gland proved it to be composed almost entirely of fatty-areolar tissue. It becomes obvious from this fact that the diagnosis of thymic hyperplasia must be reserved always until both gross and histologic studies of the thymus gland have been made.

The degree of thymic hyperplasia when it does occur in exophthalmic goiter is extremely variable. Similarly, marked variation in the degree of hyperplasia of the various components of the thymic parenchyma is also found in various hyperplastic glands.

Perhaps the most striking phenomenon in the study of hyperplastic thymus glands in the cases of exophthalmic goiter, is the occurrence in a certain number of them of thymus glands which structurally resemble those seen in infants. In the present series, twelve of the forty-seven hyperplastic glands presented this appearance. The lobular arrangement of the thymus gland in such cases is re-

TABLE I

SUMMARY OF DATA IN CASES OF EXOPHTHALMIC GOITER

Case	Age, Years Sex	Duration of Symptoms, Months	Basal Metabolic Rate	Weight, Pounds	Loss of Weight, Pounds	Significant Associated Conditions	Weight of Gland, Gm.	Histologic Appearance	Comment
1	16M	10	+38	123	12	Bronchopneumonia	48	Infantile type of thymus gland; marked degree of cortical hyperplasia, and relatively slight degree of hyperplasia of medulla; marked increase in number and size of Hassall's corpuscles; most of these revealed hyaline degeneration; a few were calcified; fibrous trabeculae were very thin.	On verge of crisis.
2	18F	4	+78 +108	130	8	Bronchopneumonia	80		Died in crisis
3	26F	30	+38	127	4	Edema of lungs	80		Recurrent hyperthyroidism
4	35F	9		80	25	Emaciation (marked)	38		In crisis
5	38M	18	+72	123	73	Edema of glottis	75		
6	39F	6		111	45	Pneumonia	65		In crisis
7	48F	4	+64	104	36	None	62		Died in crisis
8	49F	?				Empyema of gallbladder	45		Primary diagnosis, empyema of gallbladder
9	52F	2				Edema of lung	50		
10	40F	5	+110	99	11	None			
11	31F	9	+66	123	11	Purulent pericarditis	93		Acute hyperthyroid reaction postoperatively
12	26M	3	+106	116	29	Bronchopneumonia	78		
13	57F	12		100	65	None	70	Moderate degree of fibrosis and islets of marked cortical hyperplasia; slight hyperplasia of medulla with increase in number and size of Hassall's corpuscles.	Recurrent hyperthyroidism; previous ligation of thyroid arteries
14	44F	19	+32	85	15	None			
15	42F	216	+42	92	33	None	56		Exophthalmic goiter with adenomas; crisis eighteen years previously
16	45F	18	+26	180		Bronchopneumonia	30	Fibrosis, moderate degree of cortical hyperplasia, slight hyperplasia of medulla, increase in number and size of Hassall's corpuscles.	Recurrent hyperthyroidism; partial thyroidectomy twice previously
17	35F	1	+60	150	14	None	51		In crisis
18	43F	0.75			25	None	34		
19	53M	18	+41			None	43		

TABLE 1—Continued

Case	Age, Years Sex	Duration of Symptoms, Months	Basal Metabolic Rate	Weight, Pounds	Loss of Weight, Pounds	Significant Associated Conditions	Weight of Gland, Gm.	Histologic Appearance	Comment
20	40F	3	+31	110	2	Bronchopneumonia	36		
21	48F	24	+84	133	19	None		Fibrosis and large islets of hyperplastic cortical thymic tissue.	On verge of crisis
22	59M	3	+57	164	41	Bronchopneumonia			
23	22F	36	+80	150		Bronchopneumonia	98	Marked degree of medullary hyperplasia; considerable increase in number and size of Hassall's corpuscles; slight fibrosis.	
24	37M	11	+24			Diabetes mellitus			Diabetes; mild hyperthyroidism
25	72M	24	+29	88	47	Bronchopneumonia			
26	43F	132	+79			Abscess of lung			Recurrent hyperthyroidism; partial thyroidectomy three times previously
27	66M	8	+64	124	31	Bronchopneumonia			
28	47F	33	+88	110	26	Septicemia	21		
29	59F	14				None	37	Marked degree of fibrosis.	Recurrent hyperthyroidism; partial thyroidectomy two months previously
30	43F	120	+38	109	31	Pneumonia		Small islets of hyperplastic medulla with marked increase in number and size of Hassall's corpuscles; marked degree of fibrosis.	Recurrent hyperthyroidism; lobectomy previously
31	26F	3		133	27	Metrorrhagia			
32	43F	12	+147			None	8		Recurrent hyperthyroidism; partial thyroidectomies three times previously
33	32F	1.5		95	40	Bronchopneumonia	21		In crisis
34	74M	18	+37	141	56	Bronchopneumonia			
35	43F	4	+71	86	34				
36	36F	18	+35	108	37	Encysted empyema			Recurrent hyperthyroidism; lobectomy previously
37	32M	24	+86	143	22	Passive congestion			Severe hyperthyroidism
38	40M	60	+102	185		Pulmonary infarction			
39	58M	3	+61	132	63	Bronchopneumonia	24		

40	48F	6	+18	116	23	Infected hydrothorax			
41	43F	60		108	38	Bronchopneumonia			In crisis five weeks previously
42	28F	24	+56	154	11	None	52	Islets of parenchyma showing equal degree of cortical and medullary hyperplasia; increase in number and size of Hassall's corpuscles and varying degrees of fibrosis.	In severe crisis
43	53F	10	+49	88	20	None	24		
44	34F	12	+60			None	29		In crisis; recurrent hyperthyroidism; lobectomy two months previously
45	54F	7	+55	186	44	None			
46	53F	14	+33	86	39	Bronchopneumonia	11		
47	56M	42	+69	97	53	Bronchopneumonia			Postoperative hyperthyroid reaction
48	54M	4		135	30	Encephalitis (?)	148	Practically complete involution of small islets of cortical tissue	Died in crisis
49	53F	60	+53	103	47	None		Complete involution.	
50	44F	324	+39	140	25	None		Complete involution.	
51	57M	180	+54	159	25	Abscess abdominal wall	15	Complete involution.	Extremely ill; cardiac decompensation main feature
52	52F	96				Bronchopneumonia	31	Complete involution.	
53	43F	9	+83	95	28	Abscess of lung		Complete involution.	
54	47M	?	+36	135	20	Carcinoma of suprarenal gland	45		
55	62F	4	+36	106	16	Carcinoma of colon; abscess of liver		Complete involution.	

markably regular. These lobules are divided by rather thin fibrous trabeculae and there is little, if any, evidence of preëxisting involution. The cortex is rather sharply demarcated from the medulla which in most cases seems proportionately diminished in amount. The cortical tissue is considerably increased in amount, producing a rounded, bulging outer contour to each lobule. The cortex is densely packed with deeply staining, small thymic cells. In the medulla, the most striking feature is a marked increase both in the number and in the size of Hassall's corpuscles. These corpuscles vary considerably in size, some being composed of only two or three swollen, hyalinized cells, while others appear relatively huge and are composed of concentric layers of cells. Nearly every corpuscle shows an advanced degree of degeneration, the component cells being usually of hyaline character. Calcification in these corpuscles is rarely seen, and only rarely does one encounter what might appear to be recently formed corpuscles, so uniform is the process of degeneration in them. The entire picture is strikingly similar to an infantile type of thymus gland except for the marked increase in the number and in the size of Hassall's corpuscles (fig. 1).

Among the other thymus glands of this series in which hyperplasia was found, there was, besides the hyperplasia, evidence of a variable degree of preëxisting involution with a corresponding degree of replacement of fibrous tissue. In eight cases, the thymus gland showed large islets of hyperplastic cortical tissue, with a relatively slight degree of medullary hyperplasia

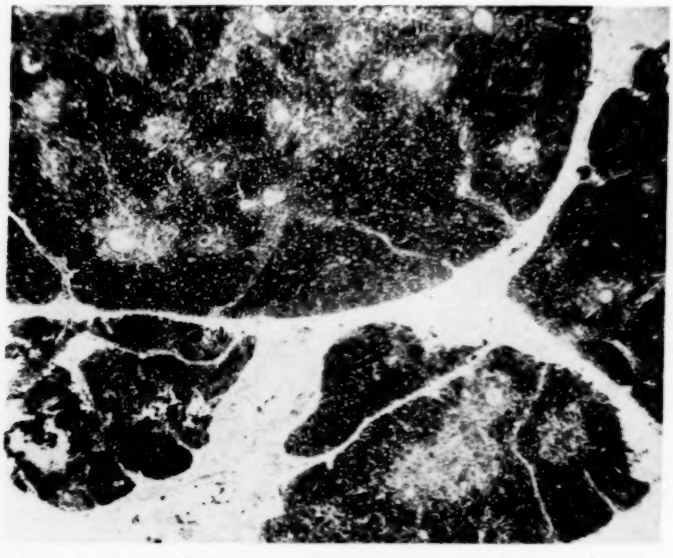

FIG. 1. Section of thymus gland of a girl aged eighteen years who died from exophthalmic goiter. There is marked hyperplasia of the cortex and little evidence of preëxisting involution (x12).

(fig. 2). These irregularly shaped islets of thymic parenchyma were separated by considerable amounts of fatty-areolar connective tissue which we must assume represent the result of the preëxisting involution. In three of these eight glands the degree of parenchymatous hyperplasia was marked, whereas in the other five glands, the fibrous tissue was more abundant and the degree of parenchymatous hyperplasia somewhat less pronounced. In all cases, there was a very striking increase in the number and in the size of Hassall's corpuscles which was identical with that seen in the infantile type of thymus gland. In two additional cases, the islets of hyperplastic tissue were represented almost entirely by cortical substance, the medulla being relatively small in amount and Hassall's corpuscles normal in size and in number.

In nineteen cases, hyperplasia was confined to the medulla, there being only a narrow rim of cortical substance bordering the islets of parenchyma (figs. 3 and 4). In seven of these cases, the degree of medullary hyperplasia was considerable and the amount of connective tissue relatively smaller in amount than in the remaining twelve cases in which the fibrosis was more marked and the islets of hyperplastic medulla correspondingly smaller in size. It is in this group of cases that the characteristic changes in Hassall's corpuscles appear in a most striking manner. In general, the changes in the corpuscles are essentially those already described as occurring in the infantile type of thymus gland. However, here the size of the corpuscles frequently assumes tremendous proportions, some being so large that they occupy the

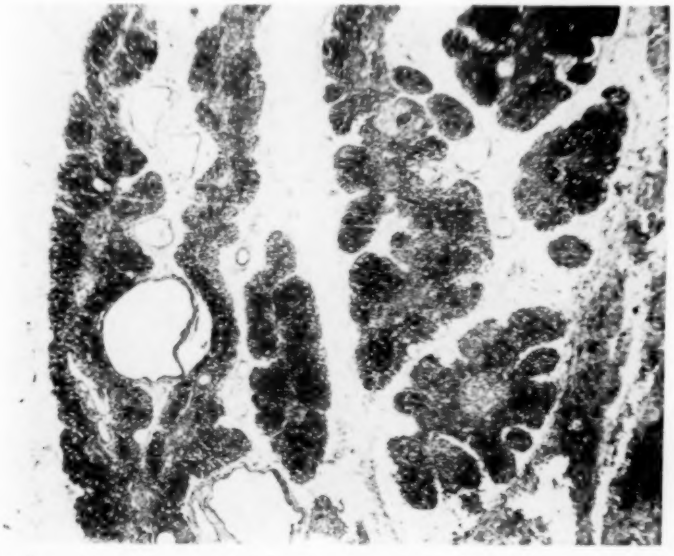

FIG. 2. Section of the thymus gland of a woman aged forty-four years who died from exophthalmic goiter. Islets of cortical hyperplasia, slight hyperplasia of the medulla, and a moderate degree of fibrosis are present (x12).

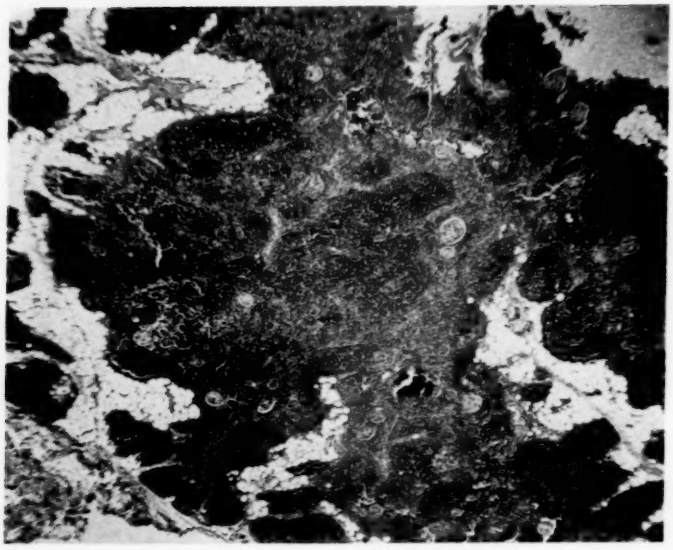

FIG. 3. Section of thymus gland showing marked medullary hyperplasia, increase in the number and size of Hassall's corpuscles and fibrosis in a girl aged twenty-two years who died from exophthalmic goiter (x12).

FIG. 4. Small islets of medullary hyperplasia and increase in the number and size of Hassall's corpuscles in the thymus gland of a woman, aged forty-three years, who died from exophthalmic goiter (x45).

greater portion of a high-power microscopic field. Frequently several corpuscles of varying sizes are found to be fused, forming conglomerate masses of hyalinized tissue in which the cellular outlines are not discernible. The degenerative process in these corpuscles must be proceeding at a rapid pace, for it is extremely unusual to find Hassall's corpuscles in which an advanced degree of hyaline degeneration has not occurred. Surprisingly, calcification of these hyalinized corpuscles is not often encountered. The reticular epithelium is quite abundant and often it is closely aggregated about well formed Hassall's corpuscles, forming concentric layers of well defined epithelium. In some cases the reticular epithelium shows widespread degeneration, the cytoplasm of the cells appearing swollen and having a glazed appearance suggesting early hyaline change. In one case such reticular epithelial cells appeared as if lying free in the epithelial network, the nucleus large and vesicular and the cytoplasm swollen and almost hyaline in appearance.

In six cases of this group, the islets of parenchyma showed an equal degree of hyperplasia in the cortex and medulla, with an increase in the number and in the size of Hassall's corpuscles, and varying degrees of fibrosis (fig. 5). Occasionally, some evidence of hemorrhage was noted within the thymus gland of patients who died shortly after thyroidectomy.

In summarizing the pathologic observations of the thymus gland in the fifty-five cases of exophthalmic goiter it may be noted that parenchymatous hyperplasia was found in forty-seven

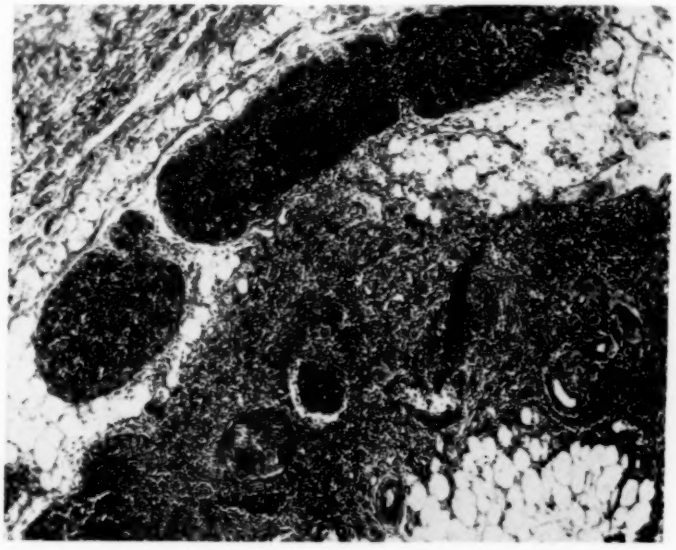

FIG. 5. The thymus gland of a woman, aged fifty-four years, who died from exophthalmic goiter. Small islets of cortical and medullary hyperplasia and marked fibrosis were present (x45).

(85 per cent). In twelve cases (22 per cent), the thymic structure resembled that seen in the thymus gland of the infant, except for an increase in the number and size of Hassall's corpuscles. In thirty-five cases, (63 per cent), hyperplasia had occurred in glands which had previously undergone varying degrees of involution and fibrosis. In the group of forty-seven cases the hyperplasia was either confined exclusively to the cortex or the cortical hyperplasia predominated in twenty-two cases (47 per cent); medullary hyperplasia was the predominant finding in nineteen cases (40 per cent), and the hyperplasia was equally distributed between the cortex and the medulla in the remaining six cases, (13 per cent). In all except two cases, in which parenchymatous hyperplasia occurred, a marked increase in the number and in the size of Hassall's corpuscles was a prominent histologic feature. Eight cases (15 per cent) showed either far advanced involution without evidence of hyperplasia or the entire thymic mass was composed of fatty areolar connective tissue (fig. 6).

Of the thirty cases of adenomatous goiter with hyperthyroidism sixteen cases, (53 per cent) showed some degree of hyperplasia, whereas fourteen cases showed advanced involution without any evidence of hyperplasia (table 2).

None of the cases exhibited the infantile type of thymus gland, so often seen in hyperplastic thymus glands of patients with exophthalmic goiter. In every instance in which hyperplasia of the thymus gland was found in cases of hyperfunctioning adenomatous goiter there was present also evidence of preëxisting involution and fibrosis. Furthermore, in all except two of the

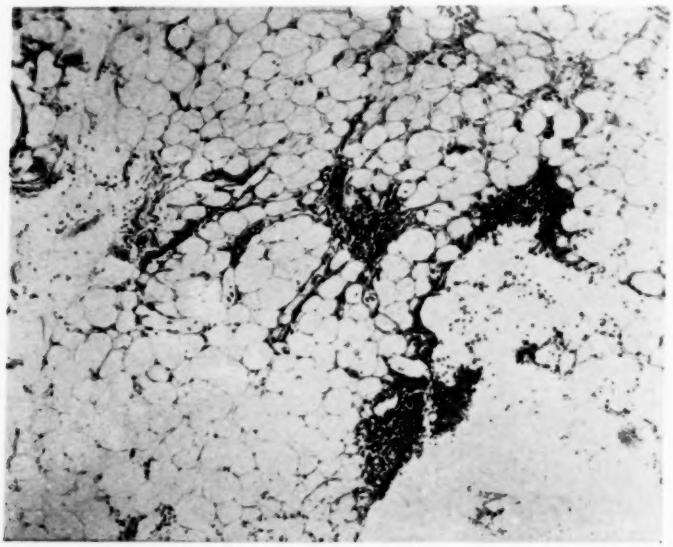

FIG. 6. Section of thymus gland of a man, aged forty-seven years who died from exophthalmic goiter; practically complete involution is shown (x50).

thymus glands of this group showing hyperplasia, the medulla alone had undergone hyperplastic change. The cortical tissue was extremely scanty in amount if, indeed, it was definitely present. These islands of medullary tissue varied in size and were separated by considerable amounts of fatty areolar connective tissue (figs. 7 and 8). In only three cases was the medullary tissue present in considerable amounts; in the other cases the hyperplastic medulla constituted only small islets of parenchyma embedded in a rather large amount of fatty areolar stroma. In addition to these cases showing medullary hyperplasia, the thymus gland in one case showed small islets of hyperplasia affecting both the cortex and medulla and in one case islets of cortical tissue alone were present, the medulla being almost entirely absent. In all of these glands in which medullary hyperplasia was present (fifteen of the sixteen glands in which hyperplasia occurred) Hassall's corpuscles were increased in number and in size. The hyperplasia of these corpuscles, the changes in their size and the tendency to degeneration was essentially identical with that seen in the thymus gland in cases of exophthalmic goiter. One exception to this was the definitely exaggerated tendency to the occurrence of calcification of Hassall's corpuscles in these glands which contrasted with the condition in the thymus glands in cases of exophthalmic goiter.

Fourteen of the thirty cases of adenomatous goiter with hyperthyroidism, (47 per cent) showed an ad-

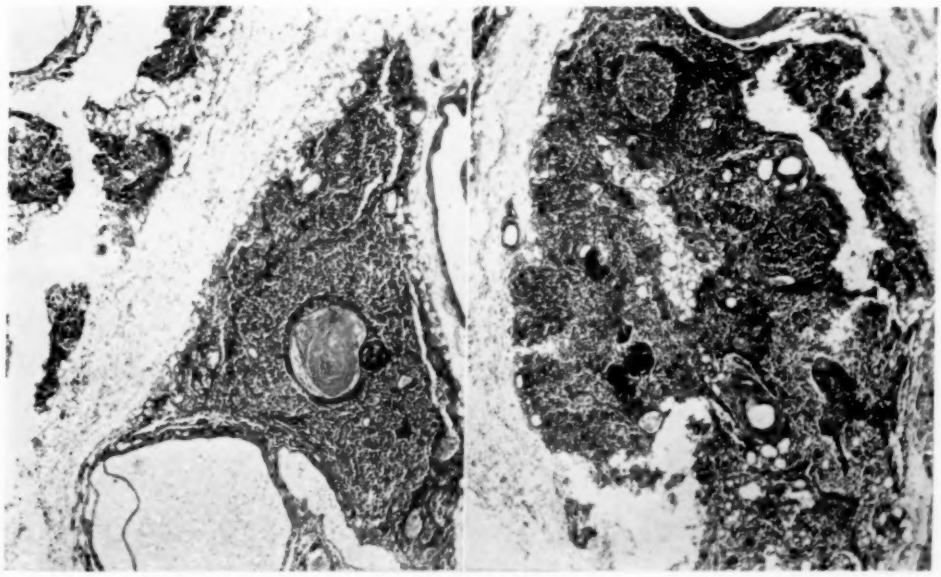

FIG. 7. Thymus gland of a woman, aged fifty-nine years, who died from hyperfunctioning adenomatous goiter. Islets of medullary hyperplasia with an increase in the number and size of Hassall's corpuscles are present (45).

TABLE 2
SUMMARY OF DATA IN CASES OF ADENOMATOUS GOITER WITH HYPERTHYROIDISM

Case	Age, Years Sex	Duration of Symptoms, Months	Basal Metabolic Rate	Weight, Pounds	Loss of Weight, Pounds	Significant Associated Conditions	Weight of Gland, Gm.	Histologic Appearance	Comment
56	59F	12		112	23	None			
57	53F	84	+28	174	1	None	9	Moderate degree of medullary hyperplasia; considerable increase in number and size of Hassall's corpuscles; marked degree of fibrosis.	
58	57F	7	+33	155	45	Pneumonia			
59	54F	1.5	+34	96	49	None		Marked fibrosis; small islets of medullary tissue containing increased number of Hassall's corpuscles many of which showed hyaline degeneration and calcification.	
60	58F	3		165	15	None			
61	64F	?	+19	122	18	None			
62	65F	24	+71	98	62	None	2		
63	38M	30	+25	149	61	None			
64	56F	24	+60	83	6	None			
65	48F	9	+56	103	117	Pneumonia			
66	51F	12	+39	130	5	None			
67	63F	60	+34	79	23	None	19		
68	55F	48	+35	154	31	None			Ligation of superior thyroid arteries previously
69	55F	1	+34	130	35	None			
70	55F	8	+31	149	36	None		Marked fibrosis; small islets of cortical tissue	
71	64F	7	+49	141	21	None		Moderate degree of fibrosis; islets of medullary and cortical hyperplasia with increased number and size of Hassall's corpuscles.	

72	59F	36	+46	186		Carcinoma of the right kidney		Practically complete involution; small islets of thymic tissue remaining
73	59F	25	+28	120	15*	Pneumonia	12	
74	47F		+40			None	18	Practically complete involution; small islets of thymic tissue remaining
75	57F	144	+52					
			+32		55	Bronchopneumonia		
76	67M	108	+43			Bronchopneumonia	39	
77	47F	15	+50	160	20	None		Complete involution; scattered small thymic cells in fatty areolar connective tissue
78	68F	18	+42	110	15	None		
79	74M	10	+32	109	66	Pneumonia		
80	49F	12	+46	125	15	Terminal pneumonia		
81	60F	48	+49	125	27	None		
82	62M	36	+25	185	47			
83	56F	48	+35	154	41	None		
84	55M	36	+61	180		None		
85	62M	24	+40	155	20	Embolic pneumonia		

Recurrent hyperthyroidism; lobectomy eight years previously
Hyperthyroid reaction postoperatively

*Emaciated

vanced degree of involution without any evidence of hyperplasia (fig. 9). In five of these glands small remnants of the thymic parenchyma could be seen, whereas in the others only occasional, scattered small thymic cells could be found. It should be noted again that among these cases in which involution was practically complete, three cases revealed glands the gross weight of which was increased. Such glands would ordinarily be assumed to constitute evidence of thymic hyperplasia if their true nature were not looked for in histologic sections.

Comment

The variability of the pathologic changes in the thymus glands in the group of cases of exophthalmic goiter and, more particularly, the contrast in the reactions between the glands in exophthalmic goiter and in hyperfunctioning adenomatous goiter, deserve consideration. For the present, one may seek an explanation for this variable reaction of the thymus gland first of all in those factors which have been proved to have definite influence on the reactions of the thymus gland.

In view of the fact that the most significant physiologic influence affecting changes in the thymus gland is that associated with advancing age, it seemed necessary to analyze the influence of this factor in this group of cases.

In the cases of exophthalmic goiter the age of the patients varied from six-

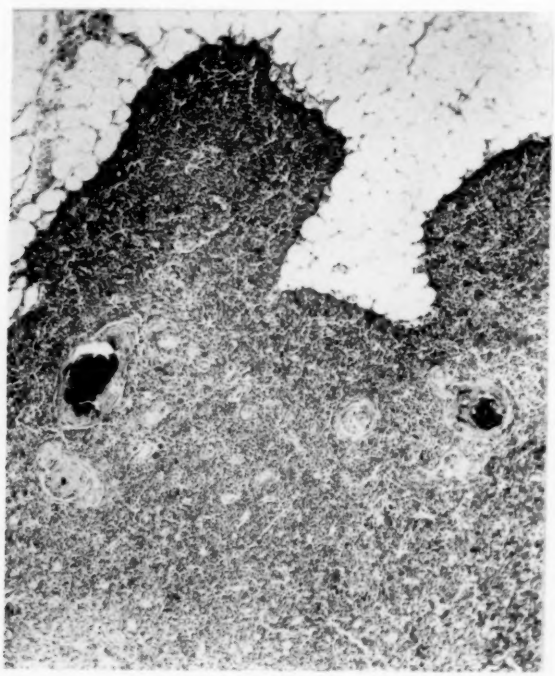

Fig. 8. Thymus gland of a woman aged fifty-seven years who died from hyperfunctioning adenomatous goiter. Medullary hyperplasia and the characteristic changes in Hassall's corpuscles may be noted (x40).

teen to seventy-four years; the average age was forty-four years. In the group of adenomatous goiter with hyperthyroidism the ages varied from forty-seven to seventy-four years; the average age was sixty years. It would seem that the more advanced age of the patients with adenomatous goiter might, to a certain extent, account for the uniformly higher incidence of preëxisting involution in the thymus gland of such patients. One might suspect that for the same reason hyperplasia of the thymus gland when it does occur in these cases is also uniformly less pronounced. That this is not, however, the entire explanation for the discrepancy becomes evident from a more detailed analysis of the age factor in the various types of hyperplasia within the group of cases of exophthalmic goiter. In the cases of exophthalmic goiter in which the hyperplasia was extremely marked, the group which showed practically no evidence of involution, the ages varied from sixteen to fifty-two years, the average being thirty-five years. This in itself points to an anomalous influence at least in certain patients with exophthalmic goiter, an influence which tends to inhibit for many years, and to a remarkable degree, the involution process of the thymus gland which normally begins at puberty. It may be noted that the average age of the patients with exophthalmic goiter, in whom parenchymatous hyperplasia occurred in glands

FIG. 9. Marked involution in the thymus gland of a woman, aged sixty-eight years, who died from adenomatous goiter with hyperthyroidism (x50).

which also showed preëxisting involution, was forty-six years. Moreover, in the cases of exophthalmic goiter in which involution of the thymus gland was the outstanding feature, the age of the patients was still higher, varying from forty-three to sixty-two years; the average age in this group was fifty-one years. Thus, it seems that in general, the age at which hyperthyroidism becomes manifest does, to a certain extent, determine the degree of preexisting involution in the thymus gland, and, similarly, the degree of parenchymatous hyperplasia. Nevertheless, there is a striking exception to this in the group of cases in which the thymus gland does not show involution even at middle age.

That disease conditions, particularly infectious processes, which may be associated with hyperthyroidism, particularly in patients who die after the operation, do not have any significant bearing on the condition of the thymus gland is apparent. It may be seen in tables 1 and 2, that in general patients with marked hyperplasia of the thymus gland had complications of an infectious nature as frequently as did those in which the thymus gland showed only slight hyperplasia or complete involution.

It is questionable whether the variable duration of the hyperthyroid state accounts for the variable condition found in the thymus gland in hyperthyroidism. Analysis of the data in the group of cases of hyperfunctioning adenomatous goiter does not yield an answer to this question, for the duration of the disease in the cases with hyperplasia was, on the average, twenty-two months, while in the cases without hyperplasia the average duration of the symptoms of hyperthyroidism was only slightly higher, namely thirty-three months. In the series of cases of exophthalmic goiter more striking data are available. Thus, the average duration of symptoms in the cases of extreme parenchymatous hyperplasia without involution was only eight and three-tenths months, in those cases in which a variable degree of hyperplasia was associated with evidence of preëxisting involution, the average duration of symptoms was twenty-nine months, whereas in cases in which hyperplasia was entirely absent, the average duration of symptoms was considerably higher, almost nine years.

Klose suggested that the explanation for the absence of thymic hyperplasia may lie in the altered nutritional state of patients who had had hyperthyroidism for a long time. Evidence obtained in my study does not support this hypothesis, although it might be suspected that the loss of weight might parallel the duration of the disease process. In fact, analysis of the data in my series of cases does not reveal any appreciable difference in loss of weight among the patients who had had hyperthyroidism for years, as compared with those in whom the symptoms of thyrotoxicosis were of relatively short duration. Neither was there any correlation between the amount of weight lost and the variable pathologic picture in the thymus gland. Thus, the average loss of weight in cases of exophthalmic goiter and marked thymic hyperplasia was 26 pounds, in cases in which the hyperplasia was associated with involution, the aver-

age loss was 30 pounds, and in those cases in which hyperplasia did not occur, the average loss recorded was even lower, 27 pounds. The same relationship holds true in the cases of adenomatous goiter with hyperthyroidism. It is obvious, then, that in my series of cases the loss of weight associated with the hyperthyroidism cannot be invoked as a cause for the variable degree of hyperplasia or involution in the thymus gland. This suggests the possibility that the duration of the hyperthyroid state causes, in some other manner, the variable pathologic picture in the thymus gland or that the variable duration of the symptoms in hyperthyroidism is, indeed, the consequence of a variable severity of the disease, dependent in turn, on a variable physiologic status of the patient, a status in which the condition of the thymus gland is but one evident index. In other words, the degree of thymic hyperplasia in hyperthyroidism, particularly in exophthalmic goiter, may be but the expression of a variable constitutional state of the patient, indicating a variable degree of susceptibility or predisposition to the development of thyrotoxicosis. The short duration of symptoms in one group of cases might then be the consequence of a more severe state of hyperthyroidism induced by a heightened constitutional predisposition to the development of this disease. The relatively long duration of symptoms may indicate a relatively higher resistance to the development of hyperthyroidism, with consequently a more benign course of the disease which permits the patient to defer seeking medical advice. This hypothesis has the merit of being most consistent with the facts in my series of cases, as I shall illustrate presently.

If thymic hyperplasia does, indeed, represent an index of a constitutional state in an individual, indicating susceptibility to the development of hyperthyroidism, then the degree of thymic hyperplasia in such cases might be expected to follow step-by-step with the severity of the disease when it becomes established. My study indicates that this is actually the case, if the severity of the disease is estimated by the incidence of thyrotoxic crisis and by the incidence of recurrence of hyperthyroidism following thyroidectomy. In the twelve cases of exophthalmic goiter in the series in which extreme hyperplasia occurred, five patients were in a state of crisis when admitted to the clinic, one patient suffered a severe hyperthyroid reaction postoperatively, and still another patient came for the treatment of recurrent hyperthyroidism which developed some time after thyroidectomy for exophthalmic goiter. In the group of thirty-five cases of exophthalmic goiter in which parenchymatous hyperplasia in the thymus gland was associated with some degree of involution, eight patients had, at some time during the course of the disease, presented the syndrome of thyrotoxic crisis, one patient had an acute hyperthyroid reaction after operation, and eight others presented recurrent hyperthyroidism following previous operations on the thyroid gland. In some of the latter, partial thyroidectomy had been performed as many as three times, with recurrence of the hyperthyroid state following each operation. Thus, of the total of forty-

seven patients with exophthalmic goiter in whom hyperplasia of the thymus gland was found, thirteen patients had been in a state of crisis, two patients had had hyperthyroid reactions postoperatively, and nine patients had had recurrent hyperthyroidism. In contrast with this is the group of eight cases of exophthalmic goiter in which involutiton of the thymus gland was found. Although the duration of the hyperthyroidism in this group was much longer than in the previous group, on an average nearly nine years, crisis occurred in only one case and in none was there a history of recurrent hyperthyroidism following thyroidectomy. Similarly, in the entire group of cases of adenomatous goiter with hyperthyroidism, in which the degree of thymic hyperplasia was uniformly less pronounced than in cases of exophthalmic goiter, a hyperthyroid reaction occurred postoperatively in one case and hyperthyroidism recurred in only one case. In both of these cases the thymus gland showed involution, which may be accounted for by the advanced age of these patients, which was seventy-four and fifty-nine years, respectively.

Thus it becomes evident that in cases of hyperthyroidism and hyperplasia of the thymus gland, particularly in cases of exophthalmic goiter, some factor tends to produce severe symptoms of thyrotoxicosis early in the course of the disease, and following partial thyroidectomy in such cases, the same factor probably tends to reproduce, in certain instances, the thyrotoxic state shortly after the operation. In cases that do not show hyperplasia of the thymus gland and in cases of hyperfunctioning adenomatous goiter, generally with only slight degrees of hyperplasia, a more benign form of the disease develops for which medical advice is not sought for years, and yet the patients remain relatively immune to the severe manifestations of thyrotoxic crisis and are less subject to recurrence of the hyperthyroidism following thyroidectomy.

My data do not permit a definite answer to the question of whether hyperplasia of the thymus gland precedes or follows the onset of the thyrotoxic state. Certain facts are, however, suggestive. In most cases in which the hyperplasia occurs, there is definite evidence of preëxisting involution, and the irregular distribution of the islets of hyperplastic parenchyma suggests that they had developed subsequent to involution. On the other hand, in the group of cases in which I have described the thymus gland as conforming, in certain respects, structurally, to the infantile type of gland, the implications are different. The lobular arrangement in such glands is so uniformly regular, the fibrous septums so thin, and the absence of much fibrous tissue so conspicuous that it seems inconceivable that this infantile structure had been reconstructed so perfectly following previous involution. The appearance of such glands makes one suspect that they had maintained their normal structure throughout the average span of thirty-five years, at which age these patients were observed at The Mayo Clinic. If this is true, the thymus gland in these cases had maintained an autonomy of existence for many years subsequent to the age of puberty, at which time

physiologic involution usually begins. The impression one gains from the study of the thymus gland in these cases of hyperthyroidism is that hyperplasia probably exists in many cases for years before the onset of the symptoms of hyperthyroidism. Some evidence which I have presented does, however, indicate that hyperplasia of the thymus gland probably occurs also following the development of the disease, as seems evident by the cases in which involution had occurred previously. The degree of hyperplasia which is maintained or the degree to which involution of the thymus gland will proceed in such cases, may depend on the variable intensity of some inherent factors in the potentially hyperthyroid state. The factors or influences which might inhibit the involution process or produce hyperplasia of the thymus gland in such cases are entirely unknown, and must, for the present, be ascribed to a certain constitution of the individual, a term the meaning of which is still somewhat vague, but one which may, in the future, be much more clearly defined. This theory is not a new one. The influence of "human constitution" in disease has been suspected for centuries. Attempts at a quantitative evaluation of this factor in disease of man is a product of modern medicine. The seriousness with which such studies are now being carried on is exemplified by such work as that of Draper and Bauer. Brown recently contributed the results of an interesting study along similar lines.

The influence of human constitution on the patient with hyperthyroidism has received some consideration in recent years. Certain observers have stressed the occurrence of lymphoid hyperplasia in patients with exophthalmic goiter. Boit, among others, reported cases of hyperthyroidism in which lymphoid hyperplasia was a prominent feature of the pathologic changes. According to Warthin, Chvostek was among the first to consider the existence of a definite constitution underlying the condition of exophthalmic goiter. From a study of pathologic material in which he frequently noted lymphoid hyperplasia within the thyroid gland and in other lymphoid structures, Warthin, too, concluded that "the constitutional defect of the thymic-lymphatic (Graves') constitution underlies every case of exophthalmic goiter and toxic adenoma[11]. That lymphoid hyperplasia is common in cases of hyperthyroidism is well known. What its relationship is to the hyperplasia in the thymus gland cannot at present be told. If it is assumed that the thymus gland is an epithelial structure, and most of the evidence seems to point to this, then it would seem logical to view lymphatic hyperplasia and thymic hyperplasia as dual manifestations of some underlying influence, rather than as an anatomically integral factor by which the hyperthyroid constitution might be symbolized.

It would be futile at this time to attempt to make any dogmatic pronouncements on the matter of the mechanism by which hyperplasia is induced in the thymus gland in cases of hyperthyroidism. It would also be futile to attempt to show the direct effect the hyperplastic thymus gland has on the thyroid gland and on the

syndrome of hyperthyroidism. The interpretation of Bircher's experimental data on inducing toxic symptoms in the dog by the implantation of hyperplastic thymic tissue, must be reserved until more is known regarding the physiology of the thymus gland in normal individuals. Knowledge of the physiologic functions attributed to the thymus gland have been gleaned from experimental studies on lower animals, and most of these have yielded contradictory evidence. In a brief critical review on the physiology of the thymus gland, Hoskins said: "Whatever be the real function of the thymus, certain it is that its production of an internal secretion has not been proved. The evidence in favor of such a theory is but circumstantial at best and very meager." In view of the largely equivocal evidence which still shrouds the results of physiologic experiments on the thymus gland, I am, for the present, entirely in accord with this view.

Summary and Conclusions

The thymus gland frequently presents parenchymatous hyperplasia in hyperthyroidism. In general, the degree of hyperplasia is much more pronounced in cases of exophthalmic goiter than in cases of adenomatous goiter with hyperthyroidism.

Cortical hyperplasia is most common with exophthalmic goiter although medullary hyperplasia, alone or combined cortical and medullary hyperplasia, also occurs. In hyperfunctioning adenomatous goiter, medullary hyperplasia is most characteristic.

An increase in the number and in the size of Hassall's corpuscles is nearly always seen in glands that show parenchymatous hyperplasia.

True hyperplasia of the thymus gland may not be inferred from an increase in its gross weight alone. Histologic studies are essential to confirm such a diagnosis.

The occurrence of hyperplasia of the thymus gland may represent the expression of a constitution indicative of an inherent predisposition to the development of hyperthyroidism. The degree of such hyperplasia may be roughly proportional to the degree of such susceptibility to the development of the disease.

It is impossible at present to evaluate the direct physiologic relationship that may exist between the thymus and thyroid glands in the syndrome of hyperthyroidism.

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The Effect of Irradiated Ergosterol on the Thrombocytes and the Coagulation of the Blood*

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IT has of course been known since the work of Zizzozero and Wooldridge that the thrombocytes are a definite factor in aiding coagulation and with their increase it has been shown by Duke[1] that the coagulation time of the blood is diminished. Gunn[2] with the ultra-violet light produced an increase of thrombocytes in rabbits. "The increase varied from 40%-100% of the original normal but always amounted to at least twice that of the normal variation in the animal." It occurred to us in considering this latter work that this action might be due to the vitamin D affected on the body surface by the irradiation. Since irradiated ergosterol offered another source of vitamin D it seemed advisable to study its effect on the thrombocytes of mammals when ingested by them in varied amounts.

Both rabbits and white rats were tried as experimental animals but we found that the control counts in the latter were more constant. Cramer, Drew and Mottram[3] have reported what they consider to be the normal thrombocyte and erythrocyte counts for white rats and our figures agree with theirs. We also tried both the direct and indirect method of counting thrombocytes and soon found the latter to be much the more satisfactory and reliable. The actual method (most of the essentials are taken from Sooy and Laurens[4]) used finally, is as follows:

(1) The rat's tail is thoroughly cleansed with soap and water and then dried.

(2) A thin coating of vaseline, to prevent any remaining particles from entering the solution, is applied to the tail.

(3) 8 cc. of the diluting fluid, described by Rees and Ecker[5], 3.8% sodium citrate, 0.2% brilliant cresyl blue, are placed in a clean 10 cc. "Wassermann' test tube.

(4) With vaseline coated scissors from 0.5 to 1.0 cm. is snipped from the tip of the rat's tail and the tail is then quickly immersed in the diluting fluid and a solution of sufficient concentration obtained. (After familiarizing one's self with the method a concentration of about the normal human erythrocyte count dilution is readily ob-

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tained. This number allows a ready discernment of the thrombocytes.)

(5) The tube is then covered with a vaseline-coated thumb of one of the investigators and inverted and reinverted for 2 minutes. (The 2 cc air bubble insures equal mixing). Care was taken to omit shaking since it was found that the results that followed were erratic. The counting chamber of a hemocytometer was then loaded with the suspension and a minimum of 400 erythrocytes and the thrombocytes in the same area counted. Each count was done in duplicate, thus checking one against the other and the average of the two used in the results.

(6) A careful erythrocyte count was also obtained from the tail at regular intervals.

(7) A silk ligature is tied around the tail about a quarter of a centimetre from the cut end to control any bleeding from the artery.

(8) The animals who were fed the irradiated ergosterol received the dosage in drops, approximately 3 drops to the minim.

Tables I and II show 2 series of 5 animals each with the initial and final erythrocyte counts and the thrombocyte counts on successive days. Table II has a group of rats who received a series of control counts 3 weeks before they received the irradiated ergosterol, as a further check on the constancy of the normal control results.

The only rat to show marked variation in the erythrocytes was No. 1 in Table I. This loss of erythrocytes we feel was most probably due to a loss of blood because of failure to tie the tail ligature properly with a subsequent hemorrhage, since the animals on whom experimental counts were first run were noticed to lose considerable blood if the stumps of the tails were not ligated.

The response to the irradiated ergosterol was just as had been anticipated. The control animals, as is seen, held a very normal variation throughout while all of the animals receiving the irradiated ergosterol increased their thrombocytes 47%-353%, depending on the dosage administered. It would seem that the rise is, at least in part, due to an actual increased production since the maximum effect is not reached for several days and the duration of the thrombocytosis is for an even greater period of time, even though the drug is discontinued. To date we have not been able to determine this satisfactorily but we are working on phases of the problem and hope to be able to report more of this at a later date.

Fig. I is an illustrative graph of the block type showing the minimum variation of the thrombocytes in the white rats before and after receiving irradiated ergosterol and the maximum variation of the control animals. (Included are the thrombocyte variations of the series studied especially for coagulation and charted in tables III, IV and V). The results here are quite conclusive but perhaps not as striking as they might have been had the second group been carried further. The first group indicated that the minimum dose tried, 3 drops, gave an excellent result and the second group was used to see if still smaller doses were effective. Unfortunately it was impossible to continue the second series for a longer period. The smaller doses

TABLE I

		1		2		3		4		5
Initial erythrocytes		8,530,000		9,575,000		8,650,000		8,265,000		8,710,000
Final "		7,030,000		9,430,000		9,010,000		8,390,000		8,980,000
Date	Dose*	Thrombocytes	Dose	Thrombocytes	Dose	Thrombocytes	Dose	Thrombocytes	Dose	Thrombocytes
3/21/29	0		0	1,116,000	0	910,000	0		0	904,000
3/22/29	0	830,000	0	1,243,000	0		0	818,000	0	889,000
3/23/29	0	736,000	0	957,000	0	895,000	0	918,000	0	750,000
3/24/29	0	833,000	0		0	1,011,000	0	860,000	0	800,000
3/25/29	0		3		10		0		10	
3/26/29	0		3		10		0		10	
3/27/29	0	779,000	3	2,064,000	10	1,829,000	0	842,000	10	1,890,000
3/28/29	0	988,000	3	1,994,000	10	1,622,000	0	971,000	10	1,300,000
3/29/29	3		3	3,520,000	10	1,482,000	0	926,000	10	1,320,000
3/30/29	3	1,660,000	3	3,240,000	10	1,720,000	0		10	1,870,000
3/31/29	0	1,931,000	3	3,720,000	10	1,508,000	0		10	1,320,000
4/ 1/29	0	1,976,000	0	4,710,000	3	1,365,000	0		10	1,370,000
4/ 2/29	0		0	5,630,000	3	1,829,000	0		10	1,675,000
4/ 3/29	0		0	3,750,000	3	2,205,000	0		10	1,742,000
4/ 7/29	0		0	2,910,000	3	1,402,000	0		10	1,450,000
4/18/29	0	1,800,000	0	2,714,000		1,264,000		917,000	10	1,146,000

*Dosage is in drops of Acterol (viosterol Mead, furnished through the courtesy of Mead, Johnson & Co.)

TABLE II

		6		7		8		9		10
Initial erythrocytes		9,995,000		10,110,000		9,170,000		9,790,000		9,750,000
Final "		9,921,000		9,900,000		9,300,000		8,960,000		9,370,000
Date	Dose	Thrombocytes	Dose	Thrombocytes	Dose	Thrombocytes	Dose	Thrombocytes	Dose	Thrombocytes
3/19/29	0		0	909,000	0		0		0	
3/20/29	0	1,320,000	0	1,060,000	0	1,070,000	0		0	
3/31/29	0	1,310,000	0	1,070,000	0	1,023,000	0	1,090,000	0	1,100,000
4/ 2/29	0		0	1,230,000	0	1,208,000	0	1,250,000	0	1,360,000
4/ 3/29	0		0		0		0	1,026,000	0	1,320,000
4/20/29	1	1,180,000	2	1,060,000	0	1,150,000	0	910,000	6	1,050,000
4/21/29	1	1,630,000	2	1,720,000	0	1,470,000	0	1,260,000	6	1,640,000
4/22/29	1	1,340,000	0	1,250,000	0	1,170,000	0	1,270,000	9	4,160,000
4/23/29	0	1,730,000					0	1,130,000	0	3,300,000

were found to be effective but they were apparently much less so in the time tried. It is particularly interesting to note that number 3 who was receiving 10 drops had a good increase but that there was an even greater increase when the dosage was decreased to 3 drops. Number 5 also had a less marked increase than rats 1, 2 and 3 indicating that too large a dose seems to have some sort of an inhibiting influence after the initial response.

The series, of course, is small, but our point, that the irradiated ergosterol did increase the thrombocytes, seemed to be proven, and with that our attention was obviously turned towards coagulation.

Previous experimental work has been done which would indicate that irradiated ergosterol should have a depreciatory effect on the coagulation time. Brougher[6] found that cod-liver oil effected a decreased coagulation time in dogs. Sooy and Moise[7] have successfully treated several patients with purpura by exposing them to the quartz light. Selye[8] has reported that when vigantol is given internally to white rats, there is an instant hastening of the coagulation time. There are no figures given in this short article.

The investigation of methods of coagulation was confined to the micro-methods since we were working with such small animals. The two methods finally selected were the Moise and Sooy[9] capillary tube method and the Boggs'[01] method. The former was finally discarded as the control re-

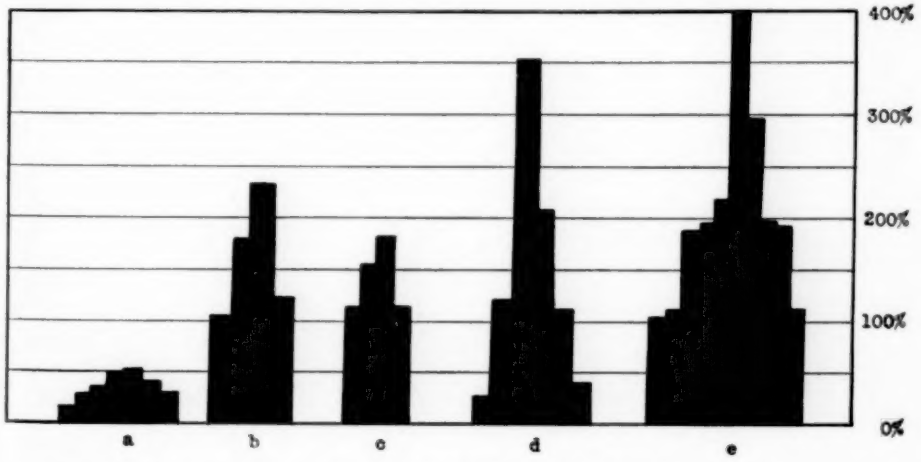

Fig. 1. Illustrative block graph showing maximal variation of the thrombocyte counts of control animals and minimal variation of animals receiving irradiated ergosterol.*

a—Control group—rat 4, 26, 9, 45, 38, 8, and 25 in order named.
b—3 drops on 3rd day—46, 31, 32, and 47 in order.
c—3 drops on 3rd and 4th day—42, 44, 41, and 43 in order.
d—Irregular doses—6, 5, 10, 2, 3, and 7 in order.
e—3 drops continuously after 3rd day—23, 35, 48, 37, 33, 24, 34, 21, 22, and 36 in order.

*The percentage results from which the thrombocytic block graphs are calculated are obtained by taking the difference between the highest and lowest thrombocyte counts as the numerator in the controls and the difference between the highest thrombocyte count before the irradiated ergosterol was administered and the highest thrombocyte count afterwards as the numerator in the test groups. (The same method is used in Fig II.)

TABLE III

			21			22			23			24	
Initial erythrocytes			9,440,000			10,120,000			9,000,000			9,060,000	
Final "			9,300,000			9,620,000			8,540,000			7,620,000	
Date	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.
10/23/29	0	482,000	2′45″	0	600,000	3′00″	0	582,000	2′30″	0	689,000	2′45″
10/24/29	0	518,000	3′00″	0	573,000	2′45″	0	568,000	2′45″	0	598,000	2′45″
10/25/29	0	443,000	2′45″	0	570,000	2′45″	3	453,000	2′30″	3	520,000	2′45″
10/26/29	3	548,000	2′45″	3	677,000	2′45″	3	545,000	2′30″	3	880,000	1′45″
10/27/29	3	711,000	1′30″	3	896,000	1′30″	3	605,000	1′45″	3	1,107,000	1′30″
10/28/29	3	960,000	1′15″	3	1,147,000	1′15″	3	855,000	1′15″	3	1,024,000	1′30″
10/29/29	3	1,335,000	1′15″	3	1,630,000	1′15″	3	879,000	1′30″	3	1,082,000	1′15″
10/30/29	3	1,402,000	1′15″	3	1,850,000	1′00″	3	1,080,000	1′15″	3	1,059,000	1′15″
10/31/29	3	1,740,000	1′00″	3	1,640,000	1′15″	3	1,150,000	1′00″	3	1,175,000	0′15″
11/ 1/29	3	1,732,000	1′00″	3	1,235,000	1′30″	3	1,240,000	0′45″	3	1,521,000	0′45″
11/ 2/29	3	2,463,000	0′45″	3	1,406,000	1′15″	3	1,285,000	1′15″	3	1,126,000	1′15″
11/ 3/29		1,715,000	1′00″		1,975,000	0′45″		1,165,000	1′30″		1,186,000	1′30″

C.T.—Coagulation time in minutes and seconds.

TABLE III

			25			26
Initial erythrocytes			8,550,000			8,730,000
Final erythrocytes			8,220,000			8,500,000
Date	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.
10/23/29	0	621,000	2′15″	0	623,000	2′30″
10/24/29	0	689,000	2′15″	0	530,000	2′45″
10/25/29	0	532,000	2′30″	0	510,000	2′45″
10/26/29	0	587,000	2′15″	0	617,000	2′30″
10/27/29	0	600,000	2′15″	0	680,000	2′30″
10/28/29	0	698,000	2′00″	0	673,000	2′15″
10/29/29	0	720,000	2′30″	0	652,000	2′30″
10/30/29	0	565,000	2′15″	0	702,000	2′15″
10/31/29	0	623,000	2′00″	0	663,000	2′15″
11/ 1/29	0	642,000	2′15″	0	678,000	2′15″
11/ 2/29	0	666,000	2′00″	0	590,000	2′45″
11/ 3/29		602,000	2′15″		601,000	2′30″

TABLE IV

		31		32			33			34	
Initial erythrocytes		7,420,000		8,790,000			9,500,000			7,440,000	
Final "		7,340,000		8,230,000			8,500,000			7,360,000	
Date	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.
11/11/29	0	900,500	1′45″	0	741,000	2′00″	0	779,500	2′00″	0	750,000	2′00″
11/12/29	0	761,000	1′45″	0	722,000	2′00″	0	625,000	2′15″	0	664,000	1′45″
11/13/29	3	905,000	1′45″	3	702,000	2′00″	3	765,000	2′15″	3	790,000	2′00″
11/14/29	0	1,145,000	1′15″	0	1,050,000	1′15″	3	1,200,000	1′45″	3	1,397,000	1′15″
11/15/29	0	1,137,000	1′30″	0	1,155,000	1′30″	3	1,208,000	1′15″	3	1,440,000	1′15″
11/16/29	0	1,033,000	1′30″	0	1,143,000	1′30″	3	1,427,000	1′00″	3	1,540,000	1′00″
11/17/29	0	2,400,000	1′15″	0	2,481,000	1′00″	3	2,245,000	0′45″	3	1,580,000	0′45″
11/18/29	0	2,466,000	1′00″	0	2,534,000	0′45″	3	1,665,000	1′00″	3	3,132,000	0′15″
11/19/29	0	1,370,000	1′15″	0	1,730,000	1′00″	3	1,327,000	1′00″	3	2,128,000	0′15″
11/20/29	0	1,005,000	1′30″	0	1,124,000	1′45″	3	1,216,000	1′15″	3	1,690,000	0′45″
11/21/29	0	983,000	1′30″	0	1,042,000	1′45″	3	1,025,000	1′45″	3	1,010,000	1′30″
11/22/29		1,170,000	1′30″		1,020,000	1′45″		1,136,000	1′45″		1,275,000	1′30″

TABLE IV

		35		36			37			38	
Initial erythrocytes		9,900,000		9,500,000			10,260,000			8,640,000	
Final "		8,220,000		9,000,000			9,320,000			8,300,000	
Date	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.
11/11/29	0	587,000	2′15″	0	1,114,500	1′45″	0	712,500	2′00″	0	625,000	2′30″
11/12/29	0	870,000	2′00″	0	1,097,000	1′45″	0	827,000	1′45″	0	715,000	2′30″
11/13/29	3	967,000	2′00″	3	1,020,000	2′00″	3	1,282,000	1′30″	0	603,000	2′30″
11/14/29	3	1,107,000	1′30″	3	1,099,000	1′30″	3	802,000	2′30″	0	475,000	2′15″
11/15/29	3	1,690,000	1′15″	3	1,280,000	1′45″	3	916,000	2′00″	0	619,000	2′00″
11/16/29	3	1,391,000	1′15″	3	1,631,000	1′00″	3	1,418,000	1′15″	0	698,000	2′30″
11/17/29	3	2,800,000	0′45″	3	1,950,000	1′00″	3	1,322,000	1′00″	0	505,000	2′15″
11/18/29	3	1,640,000	1′15″	3	3,255,000	0′45″	3	2,250,000	0′45″	0	515,000	2′15″
11/19/29	3	1,710,000	1′30″	3	2,375,000	0′45″	3	1,585,000	1′00″	0	607,000	2′15″
11/20/29	3	1,801,000	1′00″	3	1,350,000	1′30″	3	1,350,000	1′45″	0	637,000	2′00″
11/21/29	3	1,653,000	1′00″	3	1,220,000	1′00″	3	942,000	1′45″	0	655,000	2′15″
11/22/29		1,490,000	1′00″		961,000	1′30″		1,186,000	1′30″		514,000	2′15″

TABLE V

			41			42			43			44
Initial erythrocytes			10,000,000			8,600,000			8,400,000			9,630,000
Final	"		9,130,000			8,200,000			8,100,000			8,820,000
Date	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.
12/ 2/29	0	745,000	1′45″	0	626,000	2′15″	0	620,000	2′30″	0	679,000	2′00″
12/ 3/29	0	712,000	2′15″	0	560,000	2′30″	0	501,000	2′30″	0	587,000	2′15″
12/ 4/29	3	840,000	1′45″	3	444,000	2′00″	3	500,000	2′00″	3	602,000	2′15″
12/ 5/29	3	917,000	1′15″	3	1,322,000	1′00″	3	743,000	1′45″	3	965,000	1′30″
12/ 6/29	0	1,000,000	1′30″	0	1,115,000	1′15″	0	1,250,000	1′15″	0	979,000	1′45″
12/ 7/29	0	1,825,000	0′45″	0	1,230,000	1′00″	0	920,000	2′00″	0	1,108,000	1′15″
12/ 8/29	0	1,215,000	1′00″	0	1,075,000	1′00″	0	1,058,000	1′30″	0	1,236,000	1′00″
12/ 9/29	0	1,500,000	0′45″	0	1,219,000	1′15″	0	1,310,000	0′45″	0	1,425,000	1′00″
12/10/29	0	2,345,000	0′30″	0	1,230,000	0′45″	0	1,126,000	1′15″	0	1,734,000	0′45″
12/11/29	0	1,000,000	0′45″	0	830,000	1′45″	0	1,286,000	1′00″	0	1,521,000	1′15″
12/12/29	0	1,075,000	1′30″		1,012,000	1′30″		1,315,000	0′45″	0	1,202,000	1′00″
12/13/29		1,123,000	1′30″		989,000	1′30″		1,139,000	1′00″			

TABLE V

			45			46			47			48
Initial erythrocytes			8,540,000			10,300,000			8,780,000			9,150,000
Final	"		7,960,000			9,200,000			8,260,000			8,820,000
Date	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.	Dose	Thrombocytes	C.T.
12/ 2/29	0	668,000	1′45″	0	640,000	2′00″	0	678,000	2′30″	0	564,000	2′45″
12/ 3/29	0	499,500	1′45″	0	655,000	1′45″	0	702,000	2′15″	0	582,000	2′45″
12/ 4/29	0	700,000	1′45″	3	620,000	2′00″	3	664,000	2′30″	3	679,000	2′30″
12/ 5/29	0	561,000	1′45″	0	889,000	1′45″	0	790,000	2′00″	3	1,138,000	1′45″
12/ 6/29	0	561,500	2′15″	0	1,176,000	1′15″	0	976,000	1′45″	3	1,210,000	2′00″
12/ 7/29	0	558,000	1′45″	0	1,234,000	1′30″	0	964,000	1′45″	3	1,026,000	1′30″
12/ 8/29	0	650,500	2′15″	0	1,102,000	1′15″	0	1,304,000	1′15″	3	1,076,000	1′15″
12/ 9/29	0	735,000	2′00″	0	1,327,000	1′00″	0	1,573,000	1′00″	3	1,320,000	0′45″
12/10/29	0	494,000	1′45″	0	1,269,000	0′45″	0	1,310,000	1′00″	3	1,420,000	0′45″
12/11/29	0	593,000	1′45″	0	1,062,000	1′15″	0	1,239,000	1′30″	3	1,197,000	1′00″
12/12/29	0	672,000	2′00″	0	979,000	1′45″	0	1,262,000	1′45″	3	978,000	1′15″
12/13/29					1,080,000	1′30″		1,103,000	1′30″		946,000	1′00″

sults with the Boggs' method were found, in our hands, to be more consistent. The Boggs' coagulometer was hence used in all of the results tabulated below.

(1) The first 4 steps of the procedure outlined above are followed out.

(2) The tail is then wiped off with a clean cloth and the tip is touched to the upper base of the inverted truncated cone of the Boggs' coagulometer. A drop of blood is obtained which just covers the surface, i. e., the attempt is made to obtain approximately the same size of drop each time. The inverted cone is then placed in its receptacle and observed under the 16 mm. objective of the microscope.

(3) A current of air is then directed upon the edge of the drop every 15 seconds and the movement of the cells in the drop is observed with the microscope. Coagulation is assumed when the cells move en masse and spring back to their original position.

(4) Boggs' original method was modified to this extent, the stream of air was directed through a large wash-bottle immersed in a water bath which was kept between 38° and 40° C. The temperature of the incoming air was thus maintained at a practically constant temperature. The room temperature varied between 26°-27.5° C.

Three series of animals are reported. One series of 6 white rats, table III, and 2 series of 8 white rats each, tables IV and V. Erythrocyte counts were done daily and the thrombocytes determined by the indirect method described before. To evaluate the results more readily a block graph, Fig. II, is given showing the effect on the con-

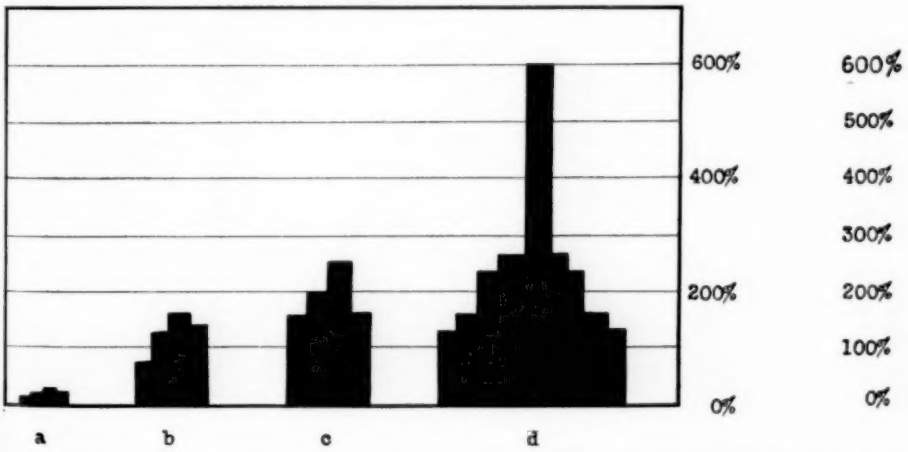

FIG. II. Illustrative block graph showing maximal variation of coagulation time* of control animals and minimal variation of animals receiving irradiated ergosterol.
a—Control group—rat 25, 26, 45, and 38 in order named.
b—3 drops on 3rd day—rat 31, 47, 32, and 46 in order.
c—3 drops on 3rd and 4th day—rat 43, 42, 41, and 44.
d—3 drops continuously after 3rd day—36, 35, 48, 21, 22, 34, 24, 23, 33, and 37.

*Obviously the coagulation time referred to here has an element, at least, of bleeding time because of the serum which will be present in the drop of blood obtained from the tail. However, just as the human erythrocyte count is assumed to be capillary blood when the flow is free, it is assumed that with free flow of blood that the majority of material obtained is arterial blood.

trol animals and on the animals receiving irradiated ergosterol. It is then seen that a dose of 3 drops on 2 consecutive days is nearly as effective as daily doses in decreasing the coagulation time but not as effective as the daily dose in increasing the thrombocytes.

Fig. III and Fig. IV are multiple graph charts of control animal No. 45 and animal No. 42, who received 3 drops of viosterol on the third and

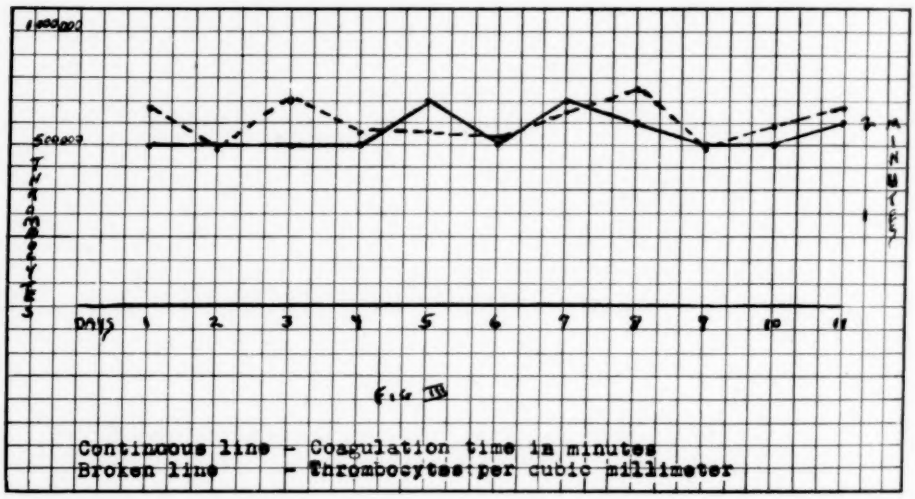
Days 1 2 3 4 5 6 7 8 9 10 11
Fig III
Continuous line - Coagulation time in minutes
Broken line - Thrombocytes per cubic millimeter

FIG. 3

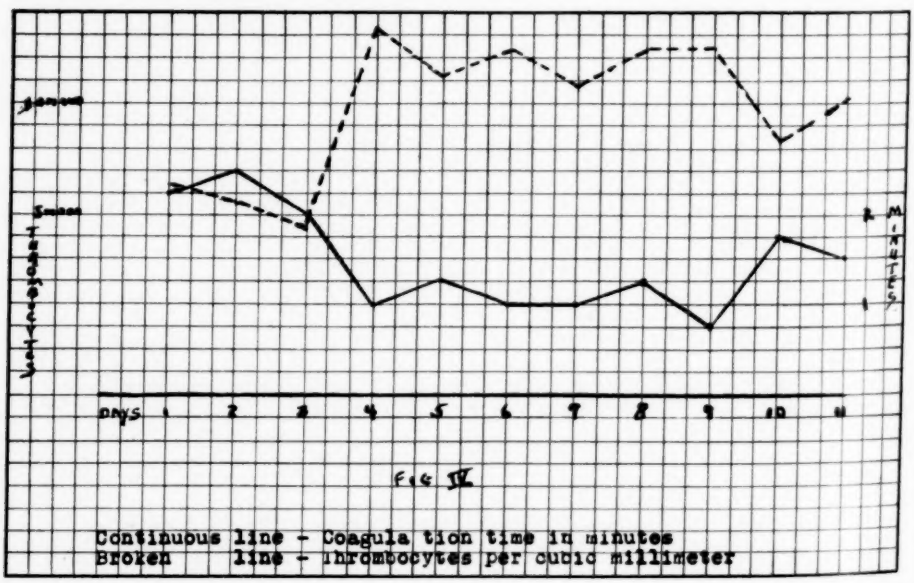
days 1 2 3 4 5 6 7 8 9 10 11
Fig IV
Continuous line - Coagulation time in minutes
Broken line - Thrombocytes per cubic millimeter

FIG. 4

fourth days only. These charts show the close association of the thrombocyte and coagulation time variations. To date sections of the liver, spleen, lung and heart of rats who have been sacrificed after receiving the irradiated ergosterol for some time have failed to show any thrombi. Consequently it would seem that a proportionate single dose could be used very effectively on surgical patients a few days before operation. Further studies on larger animals will have to be carried out to determine the exact effect on the bleeding time and the true coagulation time.

Conclusion

The tables and graphs are self-explanatory and but one conclusion is drawn, namely, that irradiated ergosterol is responsible for the increase in the thrombocytes and the decrease in the coagulation time in this series of experiments. Of course there is the possibility that non-irradiated ergosterol or other sterols will produce a like effect. This problem is now being studied and will be reported in the near future.

Further studies on the clinical dosage and its effect on the thrombocytes and coagulation time in healthy and pathological humans are now being made by Dr. L. D. Thompson and his co-workers in the Department of Medicine of Washington University, and will be reported soon.

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Failure of Irradiated Ergosterol to Relieve Parathyroid Tetany*†

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TO DATE very few reports of attempts to treat parathyroid tetany with irradiated ergosterol are available. Stern[1] tells of giving symptomatic relief to a case of fifteen years duration by administering 3-4 mg. of vigantol daily, and Brougher[2] reports four cases successfully treated with viosterol in daily doses of from four to forty drops. It, therefore, seems worthwhile to recount our experience with one case, not only because we failed to obtain results with large doses of viosterol, but because there seem to be certain theoretical reasons why irradiated ergosterol alone should not be relied upon in the treatment of parathyroid tetany.*

Tetany—With Collip's isolation of the parathyroid hormone[3] and Aub's detailed studies of its metabolic properties[4], the balance of favor seems to have swung away from the adherents of the intoxication theory of parathyroid tetany to the side of those who believe that all the phenomena can be explained on the basis of calcium deficiency. A full discussion of the various theories has been recently published by Dragstedt[5]. The most rational therapeutic measures have therefore been directed toward (a) equipping the patient with an adequate supply of the parathyroid hormone either by the daily injection of the active principle or by actual gland transplant, and (b) raising the serum calcium to its normal level directly by the ingestion of soluble calcium salts or indirectly by the application of vitamin D in its various forms. The difficulties connected with surgical transplantation of parathyroid tissue are obvious while Collip's preparation, invaluable though it is, fails to meet all requirements, because it cannot be taken orally and because, as Aub has pointed out[4], it is irregular in its effects on different persons and frequently, after prolonged administration, becomes perfectly inert. MacCallum and Voegtlin's original demonstration[6] that animals in parathyroid tetany could be rendered symptom-free by the administration of calcium salts has been so repeatedly verified in the clinic and in the laboratory that it bids fair to remain the basis for any form of therapy.

Irradiated Ergosterol—Although the classical researches of such men as

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†Since this article was written, Jacques (Surg., Gyn., and Obst., 1930, 51, 823) has published somewhat similar negative results in six cases.

McCollum, Windhaus, Hess, Steenbock and others have made it clear that in irradiated ergosterol we have been presented with an agent powerful in its ability to regulate certain phases of mineral metabolism, particularly those concerned with calcium and phosphorus, the mechanism by which it produces its effects is quite unknown. Furthermore, since rickets has occupied the attention of most investigators, there are insufficient published data on the metabolic alterations which this preparation exerts on human adults. The literature is full of testimonials as to the efficacy of viosterol in the prevention and cure of rickets[7], and infantile tetany has likewise yielded in a specific manner[8 9]. Its application to adults has been much less gratifying, however, except in osteomalacia, a disease considered to be a form of severe adult rickets, there are several reports[10 11] which indicate that lack of vitamin D is an important etiological factor. Blunt and Cowan[12] review the few observations that have been made on the effect of antirachitic substances on normal adults and conclude that moderate amounts of vitamin D have no effect upon their calcium and phosphorus metabolism, although Kroetz[13] reported that in four healthy adults he obtained an increased urinary excretion of phosphorus by adding 18-30 mg. of vigantol to a standard diet. Liu[14] obtained no benefit from cod liver oil in a case of adult tetany apparently dependent upon a functional insufficiency of the parathyroid glands, and certainly the reports of its usefulness in such varied conditions as dental caries, fractures, osteitis fibrosa cystica, tuberculosis, pernicious anemia, etc., are equivocal[15]. Recent studies[16] indicate, however, that cod liver oil is effective in checking the negative mineral balance of pregnant and lactating women. The proven therapeutic value of vitamin D is limited then to rickets, osteomalacia and infantile tetany, three closely allied disorders which, whatever their ultimate etiological factors may turn out to be, are certainly benefited by an increase in mineral retention. The evidence at hand leads one to believe that young organisms and those suffering from avitaminosis D respond to viosterol administration by an increased mineral retention, while normal adults either fail to respond at all to therapeutic doses, or, if they do, it is in the direction of an increasingly negative balance.

Mode of Action—Many theories have been advanced to explain these apparent contradictions, but only two of them seem to have sufficient data behind them to warrant consideration here. The first of these supposes that irradiated ergosterol increases the absorption of calcium from the intestinal tract, and many efforts have been made to prove that vitamin D, by lowering the pH of the intestinal contents, changes the insoluble tertiary calcium phosphate, $Ca_3(PO_4)_2$, to the much more soluble acid form, $CaH_4(PO_4)_2$. It has been realized for a long time that hydrochloric acid will partially heal rickets, and many observations[17 18 19] indicate that frequently, but not always, the feces of rachitic animals are more alkaline than normal and that vitamin D increases the acidity and lessens the amount of residual calcium of the intestinal contents. Clini-

cal determinations, however, have been even more inconstant[20]. If it should turn out to be that such changes are the essential nature of this vitamin's activity, it is conceivable that the primary alterations occur in the gastric juice, bile, pancreatic secretions, or the succus entericus. Attention must be called to a series of ingenious experiments performed by Bauer and Marble[21], which they interpret as indicating that viosterol promotes calcium absorption from the intestinal tract. Cats were fed on a low calcium diet, until it was certain that their calcium reserve was much depleted. Amputation of the left foreleg of every cat and fixation of the humeri gave them a permanent record of the state of the animal's mineral reserve at the end of the period of low calcium intake by which they could check further observations. All the cats were then given a diet high in calcium and, in addition half of them received viosterol daily. At intervals thereafter animals were killed and the bone trabeculae of the right humeri compared to those of the previously amputated left legs. In this way, they were able to see the effects on calcium storage produced by high calcium diets with and without viosterol. The authors state that in every instance not only did the high calcium diet increase the calcium reserve, but that viosterol distinctly augmented this reserve. These are certainly important observations, but one feels that they do not take into consideration possible variations in parathyroid activity.

The second theory relates the action of vitamin D to stimulation of the parathyroid glands but, like the first, is full of apparent inconsistencies. The studies of Aub and his colleagues[4] followed by those of Albright and Ellsworth[22] have shown us that an injection of parathormone in any dosage results in the following consecutive changes:—increased urinary excretion of phosphorus, diminished blood phosphorus content, increased serum calcium content, and an increased urinary excretion of calcium, the net result being a tendency toward the production of a negative mineral balance. It has not been definitely decided that the fall in blood phosphorus actually precedes the rise in serum calcium, but the increased excretion of phosphorus seems to be the primary change and the hypercalcemia may well be a secondary compensatory phenomenon. At any rate, this hormone always causes a negative calcium and phosphorus balance at the expense of the bones, a fact hardly compatible at first glance with the increased mineral retention known to occur after therapeutic doses of vitamin D[23]. While it is true that excessive doses of this vitamin produce the same chemical changes that parathormone does, the amount of viosterol necessary to cause this reversal of action is so tremendous[24 25] that the ensuing metabolic changes can hardly be compared to those seen in the clinic.

If, therefore, one is to postulate that vitamin D acts by stimulation of the parathyroid glands as Blunt and Cowan[12], Hess and Lewis[26] and Greenwald and Gross [27] have done, one must first reconcile the opposing facts that an organism given parathormone loses minerals while one given viosterol in therapeutic doses usually retains them. This Greenwald[27] has done by assum-

ing that an organism, suddenly presented with an excess of available calcium from the reservoir in his bones through the action of viosterol, will retain the excess if he needs it (pregnancy, lactation) and thus exhibit a positive balance, whereas he will reject it if the demand is not great. If this assumption is true, it would appear that parathormone should be as good an antirachtic agent as viosterol, which it is not, and furthermore, that normal adults should respond to viosterol by increased mineral excretion, which they have not been shown to do. That this theory is not entirely satisfactory is evident from the opinion of Shohl[23] that the retention of calcium and phosphorus is determined solely by the amounts of these substances in the diet and that vitamin D regulates the intermediary metabolism, "the dissolution and deposition of the bone salts." Wilder[28] too, in suggesting that rickets may be an expression of hyperparathyroidism, is driven to the opposite conclusion that viosterol works by inhibiting parathyroid activity.

Many scattered observations, however, attest to the fact that there must be some sort of intimate relationship between vitamin D and the parathyroid hormone. The following experiment of Hess has been widely quoted[26]:—viosterol given to a normal monkey on a low calcium diet raised the serum calcium effectively, but after parathyroidectomy, failed to do so. Nonidez and Goodale[29] noted that the parathyroids of chicks became enlarged when they were kept from contact with ultraviolet light on a vitamin D-poor diet. Higgins and Sheard[30] also observed that in the absence of the shorter wavelengths of sunlight chicks developed not only unmistakable hyperemia and hyperplasia, but degenerative lesions of a cystic nature in the parathyroid glands, and that these changes were considerably modified by the addition of small amounts of cod liver oil to the diet. Grant and Gates[31] on the other hand, had previously produced parathyroid hyperplasia by stimulating rabbits with ultraviolet light, and whether these experiments contradict each other or whether the lesions were essentially different in nature is difficult to say, as the different species of animals may have been an interfering factor. It would appear, however, that they are open to almost any interpretation. Pappenheimer and Minor[32] called attention to the high incidence of parathyroid hyperplasia in human rickets and thus confirmed Erdheim's original observation with regard to the same phenomenon in experimental rickets[33]. Bauer, Albright and Aub[34] and Barr and Bulger[35] have collected all the available case reports of significant enlargement of the parathyroid glands, 60% of which, according to the latter authors, have been associated with obvious bone disease, usually osteitis fibrosa cystica, rickets or osteomalacia. While von Recklinghausen's disease has not yet been classed among those due to dietary deficiencies, Wilder[28] reported partial success in treating a case of this diffuse form of cystic osteitis with ultraviolet light and a diet rich in vitamin D.

In considering a possible interpretation for such observations as these, one meets a paucity of controlled experiments which might serve to answer two important questions:—can vitamin

D increase mineral retention in the absence of normally functioning parathyroid glands, and, conversely, what are the effects of parathormone when given to an animal deprived of vitamin D? In an interesting paper Morgan and Garrison[36] call attention to these gaps in our knowledge and present experimental data which help to answer the second query. They show that in 11 young dogs fed a diet containing a normal amount of calcium and an insufficient quantity of phosphorus, but free from vitamin D, parathormone caused little response whether rickets was present or not, but that similar dogs, given viosterol also, showed an abnormally high response to parathyroid extract. They, therefore, conclude that vitamin D intensifies the activity of the parathyroid hormone, possibly by making it less easy for calcium or phosphorus or both to be excreted into the colon, and that viosterol should probably not be used in the treatment of hyperparathyroidism. Their data on total metabolic changes have not yet been published but will, it is hoped, shed light on this puzzling question of why an agent like viosterol, which is known to increase mineral retention under the precise conditions of their experiment, should not be used to check the demineralizing process of hyperparathyroidism. Such clinical results as Wilder's[28] lead one to believe that it may actually be beneficial.

Data pertaining to the first question are considered experimentally by Greenwald and Gross[27]. It would seem an easy matter to remove the parathyroids from animals and then to observe the effects of vitamin D therapy, but those who have attempted to control parathyroid tetany by this means, report contradictory results. Jones[37] found that cod liver oil given preoperatively to parathyroidectomized dogs usually prevented tetany, and has recently reported[38] that irradiated ergosterol also will not only prevent tetany under similar circumstances, but will produce hypercalcemia if given postoperatively. He used this drug in daily doses of 50 mg., however, which would imply that adult humans might require something over 100 c. c. of the usual commercial preparations daily, an absolutely prohibitive amount. Brougher, too,[39] found that the decline in serum calcium and the onset of symptoms were delayed and less severe if cod liver oil was given even postoperatively; later[40] he concluded that irradiated ergosterol afforded similar protection. Liu[14] however, got no results in a case of idiopathic hypoparathyroidism with cod liver oil, and Urechia and Popoviciu[41] as well as Greenwald and Gross[27] failed experimentally with viosterol, the latter even when large amounts of calcium were used. These authors point out the technical difficulty of removing all parathyroid tissue, and harmonize these conflicting results by predicating that residual parathyroid tissue, stimulated by vitamin D, will sometimes be sufficient to prevent tetany. If this theory is correct, it is easy to see that those cases of parathyroid tetany with a relatively large amount of residual parathyroid tissue will respond to treatment with viosterol, while those more severe cases in which the amount of functioning glandular tissue is presumably already working to full capacity will not.

Obviously, then, neither theory is supported by decisive evidence and very likely, as our knowledge increases, it will be found that neither one is wholly true. The chief objection to the theory that vitamin D increases calcium absorption from the intestinal tract is that it is not proved; it rests upon chemical possibilities. The second theory is perhaps more attractive because of the undoubted relationship that exists between the parathyroid glands and certain bone diseases, but there are inconsistencies that prevent its ready acceptance. If the vitamin serves only to stimulate the parathyroids to greater secretory activity, it is fair to assume that parathormone should possess antirachitic powers also, properties which have never been claimed for it. Furthermore, if it is agreed that viosterol leads to increased mineral retention in young animals or in those whose demand for calcium is greater than normal, it should follow that parathormone will also cause a negative calcium balance to become normal under these conditions. The opposing effects upon mineral balance of parathormone and irradiated ergosterol are difficult to reconcile on the theoretical assumption of a given animal's need for calcium. The complicating factors are many and intricate, and one feels that until more is known about phosphorus metabolism particularly, such theories as these will remain only theories. In the meantime, there are apparently no other more suitable hypotheses to work on.

When one attempts to apply all this to the treatment of disturbances of mineral metabolism, the confusion becomes all the greater. One is tempted, for instance, to try to check the negative calcium balance of hyperparathyroidism with viosterol, but hesitates to do so with the theory in mind that the patient might be made worse by thus stimulating the parathyroids to even greater activity. Conversely, since a tetanic organism is already in positive mineral balance, it might be supposed that viosterol would make the situation the more acute by increasing the retention further, although advocates of the hormone-vitamin theory would probably anticipate benefit from stimulation of residual gland tissue. Certainly, more data are urgently needed.

Case Report

The admission of a woman to the hospital wards gave us an opportunity to try viosterol therapy and to get what information we could which might support one theory or the other. Unfortunately, the mental condition of the patient was such that it was impossible to obtain anything like complete metabolic studies so that our data are limited to blood studies, the value of which is admittedly limited.

Mrs. L. P., a 29 year old Scandanavian housewife, was admitted to the medical wards of the hospital of the University of Michigan in March, 1930, because of repeated convulsions. Lingual difficulties and the low mental status of the patient precluded a full and accurate history, but it was learned that 12 years previously, she had undergone an operation for goitre in another city. Two weeks after leaving the hospital there, she had an attack of generalized muscular rigidity accompanied by coma, cyanosis, foaming at the mouth, biting of the tongue, and urinary incontinence. Since then, she had had countless numbers of similar episodes. They came on without aura or known cause, and usually lasted five or ten minutes, having been particularly frequent during the menstrual periods when she had had as many as seven in one day. Her husband denied ever having noticed that her hands assumed a position that might be in-

terpreted as carpo-pedal spasm or that she had ever cried out in a manner to suggest laryngospasm. Following such an attack, she always felt weak, but had no pain or headache.

During this period of 12 years, she bore two children without difficulty; during the pregnancies and succeeding periods of lactation she was, curiously enough, entirely free from attacks. Her finger nails are stated to have fallen off five times since her operation, and she had a great deal of trouble with her teeth which had become very soft. For the past three or four years, her vision had failed rapidly until, on admission, she was barely able to distinguish one object from another. No parathesias were complained of.

Her past history was apparently uneventful, except for influenza in 1918 and pneumonia in 1929. She had had a spontaneous miscarriage in 1927. She and her husband denied any fits or mental trouble prior to her operation for goitre, but a family friend told us that the patient had often had periods of irresponsibility since girlhood. The family history was unimportant.

Physical examination revealed the following important items:—(1) Each eye showed many radiating lenticular opacities of the mossy type, most marked in the nuclear regions, (2) dental caries of an unusually severe degree, (3) a thyroidectomy scar of the usual collar type, (4) marked dystrophy of the finger nails characterized by deep transverse folds and extreme brittleness, (5) a strongly positive Chvostek's sign and (6) an easily demonstrable Trousseau phenomenon.

Laboratory studies revealed a slight secondary anemia, the erythrocytes being 4,190,000, the hemoglobin (Sahli) 73%, the leucocytes 7,950 and the differential smear entirely normal. The serum calcium was 7.9 mg. per 100 cc. serum. The blood inorganic phosphates were 5.8 mg. per 100 cc. plasma. The fasting blood sugar was 102 mg. per 100 cc. The routine diagnostic blood Kahn tests were repeatedly 3 or 4 plus, but the spinal fluid was entirely normal. The basal metabolic rate was plus 1%. The urine and stools were both normal. X-ray plates of the skull and long bones were negative and revealed no striking change in lime density. Stimulation of the ulnar nerve resulted in a cathodal opening contraction with 2 milliamperes of galvanic current.

The diagnosis was latent parathyroid tetany, epilepsy of the grand mal type and latent syphilis. The character of the convulsions together with the striking fact that the periods of pregnancy and lactation represented the only intervals of freedom from them convinced us that they bore no relation to the parathyroid deficiency, although Gibson[42] quotes Redlich as having collected 72 cases in which epilepsy accompanied or followed tetany. There were no clinical signs of active lues, and we felt that syphilitic epilepsy in the face of a normal spinal fluid was a remote possibility.

Clinical Course—The patient was almost immediately given 1 cc. of viosterol (Parke, Davis and Company) morning and night. This preparation is valued at 100 D, and is stated to contain about 0.7 mg. of irradiated ergosterol per cc. No other medication was given and she received the usual ward diet without restrictions. After ten days of this regime, her serum calcium had fallen from 7.8 to 6.1 mg. per 100 c. c., and at the same time the inorganic phosphates of the blood had risen from 6.0 to 6.9 mg. per 100 c. c. These events did not seem to indicate increased calcium absorption and she maintained the signs of latent tetany which she presented on admission. An attempt was then made to study her mineral metabolism in accordance with the methods outlined by Aub[43]. A diet was kindly prepared by Miss Ina Stevenson, hospital dietetian, which contained an average daily ra-

tion of 0.1 gm. of calcium, 0.5 gm. of phosphorus, 2-3 gm. of NaCl, sufficient protein to keep the patient in nitrogen equilibrium and enough calories to prevent loss of weight. At this point, however, seizures became so frequent and the patient so completely out of hand that all attempts to collect excreta or to measure accurately food consumption became out of the question. The low calcium diet was continued, however, since it allowed a more accurate estimation of calcium intake; the patient never took more and usually received less than the calculated amount.

This psychosis was classifiable only as a mixed psychogenic reaction. She rather rapidly developed a complete disorientation accompanied by hallucinations, great apprehension and periods of hypomania alternating with short intervals during which she would lie passively in bed with her eyes fixed to the ceiling, but in constant lateral nystagmus. During these quiet periods, she would cooperate well and insist that she felt entirely comfortable. The reflexes were equally sluggish throughout and no pathological ones were obtained. She was completely incontinent of bladder and bowel. Seizures were frequent, but neither the number of convulsions nor the degree of psychosis bore any apparent relation to the level of serum calcium. Fünfgeld,[41] however, has described definite tetany psychoses.

In spite of the lowered calcium intake, no further change of any magnitude took place in the blood calcium or phosphorus levels during the next two weeks. In accordance with the suggestion of Dr. Walter Bauer, who was kind enough to see this patient with us, the following study of calcium absorption was made. The patient, having been without viosterol or other medication for two weeks, and having been on the low calcium diet for one week, was given by mouth 10 gm. of calcium-gluconate, a compound containing about 10% calcium and free from disturbing acid-producing properties. The fasting serum calcium was determined beforehand and deviations from it followed by withdrawing blood every hour for six hours after ingestion of the gluconate, and then at 9, 12 and 24 hours. Later, viosterol was administered under the same conditions in daily doses of 20 cc. for two weeks, and the same test repeated. The two absorption curves are shown in Figure I.*

We have only one conclusion to draw from these two curves and that is that, in this instance, large doses of viosterol did not increase the absorption of calcium from the intestinal tract. It will be noted that after the administration of viosterol, the initial level of calcium is slightly elevated. That this probably does not mean increased calcium absorption is shown by the absence of any post-ingestion rise; it might be explained on the basis of parathyroid stimulation and doubtless this woman had residual gland tissue, else her tetany would have been more manifest. We have no explanation for the absence of the post-ab-

*Miss Mary L. Stanley very kindly performed all blood chemical determinations. The Clark-Collip modification of the Kramer-Tisdall method was used for estimating the serum calcium, and the Fiske-Subbarow method for blood inorganic phosphate.

sorptive rise in the second instance, but feel that it is an indication that the vitamin D medication did not augment mineral absorption in the intestinal tract.

At this point, because of the patient's mental condition, she was transferred to another institution where it is hoped that she can be followed. Before discharge, her blood calcium and phosphorus levels were restored to their normal levels by injections of parathormone and the signs of increased nerve irritability disappeared for the first time. Since she was a relatively mild case of tetany, it was thought that she would probably do well on large doses of calcium by mouth, however, so that parathormone was discontinued on discharge, and the patient equipped with calcium lactate. The slight rise in serum level produced by viosterol in the second test prompted us to prescribe this substitute also.

Conclusion

(1). A case of parathyroid tetany associated with epilepsy and acute psychosis is reported.

(2). The theories of the action of irradiated ergosterol are briefly described and evidence is presented to show that one of them which supposes that vitamin D increases calcium absorption from the intestinal tract is not supported.

(3). The mechanism by which irradiated ergosterol acts is not known. It seems highly improbable that it stimulates the parathyroid glands to increased secretory activity.

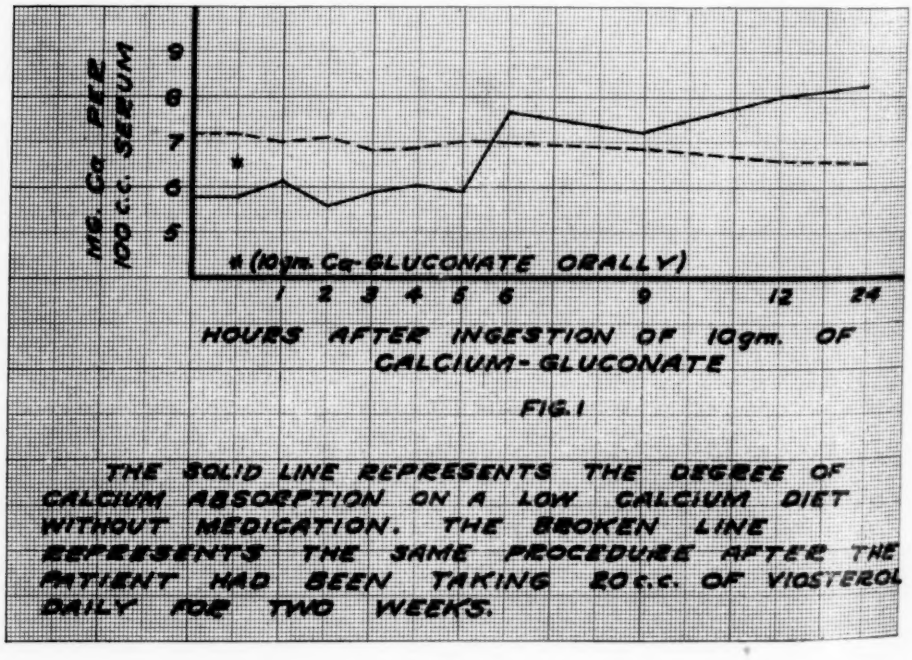
MG. Ca PER 100 C.C. SERUM
9
8
7
6
5
* (10 gm. Ca-GLUCONATE ORALLY)
1 2 3 4 5 6 9 12 24
HOURS AFTER INGESTION OF 10 gm. OF CALCIUM-GLUCONATE
FIG. 1
THE SOLID LINE REPRESENTS THE DEGREE OF CALCIUM ABSORPTION ON A LOW CALCIUM DIET WITHOUT MEDICATION. THE BROKEN LINE REPRESENTS THE SAME PROCEDURE AFTER THE PATIENT HAD BEEN TAKING 20 c.c. OF VIOSTEROL DAILY FOR TWO WEEKS.

Fig. 1

(4). Large doses of viosterol alone are insufficient treatment for parathyroid tetany, and it is thought that even if it be combined with calcium therapy, the viosterol is an unimportant factor.

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Recovery from Streptococcus Meningitis*

Report of a Case and an Analysis of Reported Cures.

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IT requires no brief to substantiate the statement that streptococcus meningitis is ordinarily a fatal disease. Clinical contact with any type of suppurative meningitis, excepting perhaps the meningococcus, has taught us the gravity of this type of illness. The mortality for the streptococcus form is exceedingly high and cases of recovery, although they do occur from time to time, are rare enough to be always worthy of interest.

We present a case of recovery and a study of reported cases of cure. Although we have carefully attempted to review all the pertinent literature, we cannot help but feel that possibly additional cases of recovery have been overlooked. Numerous references have been studied in which only diplococci have been reported, with no further description of the organism found. Unless specified to the contrary, we have assumed the bacteria to be the meningococcus or probably the pneumococcus. Such cases have, of course, been omitted from further consideration. By far the greatest amount of work on the subject of purulent meningitis has been done by otologists. Comprehensive studies are found in the literature of almost all countries, particularly in Germany.

We believe that any additional instance of a case which survives streptococcus meningitis should serve to stimulate a careful study of the surrounding circumstances. The therapy employed should be analyzed with the view that a rational empiric, if not a specific, therapy may be ultimately evolved. Particularly is recovery rare when, as in our case, the meningitis is unrelated to any remediable source of infection.

Case Report

M. B., aged 6 years, was admitted to the Brooklyn Hospital February 23, 1929, complaining of backache, fever, and pain in the back of the neck. Six weeks prior to admission she had had a slight cold with sore throat, accompanied at the time by chills, fever and vomiting. The vomiting was described as projectile in nature. For four weeks the condition had abated little; there were still recurrent chills, fever, headache and vomiting, and two weeks before admission the child developed a stiff neck with constant pain in the back.

Previous History: The patient's general health had been good. She had measles at the age of two; otherwise no infectious or contagious diseases. The father, mother and five other children were living and well.

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Physical Examination: Showed a fairly well developed and well nourished girl, lying in bed, acutely ill, crying and complaining constantly of headache and pain in the back.

There was marked rigidity of the neck to a degree that no forward bending was at all possible. The pupils were equal, reacted to light and accommodation; there was no nystagmus or strabismus. The knee-jerks were hyperactive. There was no Babinski sign or Gordon or Oppenheim. No ankle clonus. The Brudzinski sign was positive. Kernig's sign was bilaterally present.

There was no mastoid tenderness; both ear drums were normal. There was herpes on the lips; the tongue was coated; the pharynx was red and injected; the tonsils were small, cryptic and infected. Slight cervical lymph node enlargement was present. There was no impairment of resonance in the lungs; breathing was vesicular; no râles were heard. This heart was normal, the rate rapid but regular; no murmurs were present. The abdomen was slightly distended; there was no tenderness and no masses were felt. There was marked anterior bowing of both tibiae, with suggestive sabre shaped surfaces.

Urine examination showed a heavy trace of albumin, but no sugar; many pus cells were present microscopically. The white blood cell count was 20,000, with 68 per cent polymorphonuclears, 32 per cent lymphocytes; red blood cells 4,350,000; hemoglobin 68 per cent.

February 23rd (day of admission): Lumbar puncture was done and 50 cc. of cloudy fluid obtained, showing a cell count of 2435 per cmm., almost all polynuclear cells, globulin two plus (++), sugar slightly decreased. No organisms were seen on smear. 10 cc. of a concentrated preparation of a commercial antimeningococcus serum were given.

February 24th: Lumbar tap was repeated twice during the day with the removal of 40 cc. at 10 A. M. and 52 cc. at 6 P. M. of cloudy spinal fluid. 35 cc. and 38 cc. of antimeningococcus serum were injected following each tap, respectively. No organisms were demonstrable on smear. The patient's condition was poor; she cried frequently during the day, was restless, irritable, and vomited once; she took fluids very poorly.

February 25th: The child was extremely restless; her condition appeared to be getting worse. Three lumbar punctures were done this day. At 2 A. M., 50 cc. of cloudy fluid were removed and 35 cc. of antimeningococcus serum were given. At 4 P. M., 40 cc. were removed and 20 cc. of serum given. At midnight, 35 cc. were removed and 20 cc. of serum given. No organisms were demonstrable on smear. The cultures were still sterile.

February 26th: The patient had become very restless and cried out a great deal. The opisthotonos had become marked. In an effort to relieve pressure, three lumbar punctures were done again on this day. At 10 A. M., 30 cc. were removed and 20 cc. of serum given. At 5 P. M. 23 cc. were removed and 20 cc. of serum given. At midnight 42 cc. were removed and 20 cc. of serum given.

February 27th: The patient appeared to be a little more quiet, although still complaining of severe pain in the head and in the legs. At 8 A. M., 20 cc. of spinal fluid were removed and 15 cc. of antimeningococcus serum given. A long chain streptococcus was demonstrated in direct smear of this fluid, and in the afternoon the culture of the second day's fluid was reported as containing a partial hemolytic streptococcus. At 9 P. M., 30 cc. of turbid spinal fluid were removed and 15 cc. of a commercial antistreptococcus serum given.

February 28th: There was little change in the extreme condition of the child. Opisthotonos was marked. Feeding was done with difficulty. A hemorrhagic rash was present on the body. At 9 A. M., 45 cc. of turbid spinal fluid were removed and 18 cc. of antistreptococcus serum injected. At 7 P. M., 30 cc. of turbid spinal fluid were removed and, before injecting 15 cc. of antistreptococcus serum, the canal was irrigated with about 20 cc. of 1-4000 aqueous solution of neutral acriflavine.

March 1st: Restlessness continued; the head was markedly retracted. Two lumbar punctures were done. At 9 A. M., 45 cc. of turbid spinal fluid were removed, the canal irrigated with 1-4000 acriflavine solution, and 10 cc. of antistreptococcus given. A long chain streptococcus was present in the smear. At 10 P. M., 25 cc. of turbid spinal fluid

were removed and the spinal canal irrigated with 1-4000 acriflavine; no antistreptococcus serum was given.

March 2nd: The child's condition was worse. She had an involuntary bowel movement. Her head was markedly retracted. Two lumbar punctures were done, one at 9 A. M. with the removal of 35 cc. of cloudy fluid, and another at 10 P. M., when 25 cc. were taken off. On both occasions the canal was irrigated with 1-4000 acriflavine and 10 cc. of antistreptococcus serum were given only after the morning puncture.

March 3rd: The patient's condition was little changed; she swallowed with difficulty. At 11 A. M., 36 cc. of cloudy spinal fluid were removed, the canal irrigated with acriflavine, and 10 cc. of antistreptococcus serum given. The cell count was 4300 per cmm., almost all polynuclears.

March 4th: There was some improvement in the patient's general condition. Her head was slightly less retracted. The blood culture was sterile. At 9 A. M., 20 cc. of cloudy fluid were removed and the canal irrigated with acriflavine solution; no serum was given. The cell count was 1200 per cmm.

March 5th: There was little change in the patient's condition; she was still having difficulty in swallowing. Only 3 cc. of turb'd spinal fluid could be obtained on puncture. Irrigation of the canal, however, was possible and, after 12 cc. flowed in by gravity, 24 cc. of yellowish turbid fluid were removed. Apparently a block had been broken through. No serum was given.

March 6th: The patient's condition was better; she was able to swallow. No fluid could be obtained in the morning lumbar puncture, but at 7 P. M. about 1 cc. of yellowish but clear fluid was removed. Again the canal was irrigated with acriflavine solution. No serum was given. The cell count was not done.

March 7th: The patient was very restless and talking continually. On lumbar puncture, only 5 cc. of clear yellowish fluid could be obtained; it contained 25 cells per cmm. Failure to rel'eve pressure by the lumbar route and the continuance of extreme rigidity and restlessness, made removal of fluid by cistern puncture advisable. Under gas-oxygen-ether anaesthesia, 33 cc. of clear watery fluid were obtained, containing only 55 cells per cmm., chiefly polynuclears. 10 cc. of another commercial brand of antistreptococcus serum were given. The spinal fluid gave a normal reduction for sugar.

March 8th: Patient's condition was much improved; she slept well during the night. Only 2 cc. of fluid could be obtained by the lumbar route, but it was watery clear. A normal reduction test for sugar was present.

From this time on, the child's general condition improved, though slight temperature persisted. She was mentally brighter, answered questions intelligently, but the retraction of the neck persisted. No further lumbar taps were done.

March 12th: The blood Wassermann was negative.

March 16th: The patient was greatly improved and was put out on the porch; was able to take solid food. The retraction of the neck was improved; her temperature was normal.

March 25th: Patient was able to sit up in bed. Her neck was no longer stiff. She looked well, though drawn and somewhat pale.

March 27th: She was out of bed for the first time in a wheel chair.

April 1st: Patient was up and about. There was no impairment of her gait; no residual disturbances in the central nervous system were apparent. Her recovery appeared excellent.

April 11th: Throat culture showed long chain streptococcus.

April 12th: The blood Wassermann was three plus.

April 19th: The blood Wassermann was two plus.

Just prior to discharge, examination revealed the following:

The eyegrounds showed no pathological changes; normal vision was present in both eyes. The intradermal tuberculin test (1/10 mgm.) was negative. X-ray examination of the teeth showed no abscesses present, though dental caries was present in the upper molars. The nasal sinuses were clear; the mastoid cells were not clear on either side, perhaps due to lack of development, though more

FIG. 1. Photograph taken March 5, 1929, showing extreme opisthotonus. A hemorrhagic rash is visible on trunk and extremities.

differentiation at her age would be expected.

Neurological Examination. She understood and performed all tests well. The cranial nerves were normal. The pupils reacted to light and accommodation; fundi were normal. The reflexes were normal. There was no Kernig and no rigidity of the neck. There was definite tremulousness of the muscles of the lower extremities, particularly when the leg performed gross movements. No mental impairment was evident. The Binet-Simon and Pintner-Cunningham tests were done; both averaged her mental age at about 7 years, which was her approximate chronological age.

April 17th: The patient was discharged, apparently entirely well, 54 days after admission.

Summary

Streptococcus (partial hemolyticus) meningitis with complete recovery in a girl age 6. The onset followed an acute sore throat and upper respiratory infection, and the illness ran a long course. The treatment consisted of repeated lumbar punctures and spinal canal irrigations with 1-4000 neutral acriflavine aqueous solution and antistreptococcus serum injections. Cisterna puncture became necessary on one occasion, when block had apparently developed. Recovery was slow but complete.

Comment

The significance of the positive blood Wassermann reaction on two occasions is difficult to determine. Aside from the suggestive sabre-shaped tibiae, there were no signs of lues. The serological findings will bear re-checking and specific treatment will be instituted if positive results are obtained. The relation of the possible presence of lues to the meningitis, however, seems purely incidental, but it is of importance when one is trying to estimate and correlate the factors which may influence the prognosis.

The use at first of antimeningococcus serum, before any organism was isolated, followed later by specific antistreptococcus serum and still later by acriflavine aqueous solution (1-4000) canal irrigations, makes it difficult to determine with any degree of accuracy the value of any or all of the therapeutic agents employed. It does not seem likely that the antimeningococcus serum could have been of benefit, except perhaps as a foreign protein. Clinically at least, no improvement was noted during the period when antimeningococcus serum was used; actually, the patient had grown worse. No improvement was noted with the antistreptococcus serum until the acriflavine irrigation was instituted, at first in combination with the serum and later alone. Whether recovery, when it occurs, proceeds spontaneously and irrespective of treatment, there is no way of judging, but, in our own case at least, clinical improvement began and progressed under a combination at first of antistreptococcus serum injections and neutral acriflavine solution irrigations, and later with acriflavine irrigations alone.

Summary of Reported Cases

Despite the rarity of recovery, we have been able to gather from the literature a record of forty other instances of recovery from streptococcus meningitis.

Historical: Though recent writings credit the first reported instance of recovery to Alexander, in 1908, Schenke and Streit reported a case in 1901;

FIG. 2

FIG. 3

FIG. 2. On discharge from the hospital, April 17, 1929.
FIG. 3. Appearance of patient, September 26, 1929.

Schulze published one in 1903; Gruening told briefly of a case before the New York Otological Society on March 22, 1904 and Voss published one in 1905. In the case published by Schenke and Streit, however, it must be said that only one streptococcus was seen on smear; the spinal fluid, however, was turbid. Thereafter came Alexander, in 1908, with two cases; Netter with one in 1909; one by Graef and Wynkoop and one by Mygind in 1910; Tedesco and Ohnacker each recorded one case in 1911. From 1911 to 1920 inclusive, 13 cases were reported, and from 1921 to the present there were 17 cases, including our own.

Age: Of the 41 cases, the age is not given in only one instance.

Under 2 years	1
2 years	1
5 years	2
6 years	2
7 years	4
8 years	2
10 years	3
11 years	1
12 years	3
13-20 years	6
21-25 years	5
26-30 years	2
31-35 years	2
36-40 years	2
41-45 years	1
46-50 years	2
65 years	1

Fifteen, or 37.5 per cent, occurred in the first decade of life; ten, or 25.0 per cent in the second decade; seven, or 17.5 per cent in the third decade; four, or 10.0 per cent, in the fourth decade and four, or 10.0 per cent, after the age of 40.

One can only postulate on the reasons for the high incidence in early life. One factor that would seem to suggest itself is the greater frequency of otitic infections during this period. Actually, otitis media, as will be shown shortly, was the inciting cause in 66.6 per cent of all cases. After the age of thirty, recovery is relatively rare, but, lacking statistics of occurrence in a large series of cases, it is of little value to attempt any conclusions as to percentage mortality for any given age group.

Sex: In one instance the sex is not stated. Of the remaining cases, twenty-three were males and seventeen females.

	Male	Female
Under 2 years	1	0
2-10 years	4	10
11-20 years	7	3
21-30 years	5	2
31-40 years	3	0
41-50 years	2	2
Above 50 years	1	0

Though the general incidence is somewhat higher in males, it is striking that in the first decade there are twice as many females as males who recovered.

Source of Infection: In twenty-eight, or 68.3 per cent of the cases, the source of infection was directly traceable to otitis media, rarely alone and most often in combination with mastoiditis. In one case (Alexander) the otitis was associated with an extradural abscess. In four instances (Voss, Neal and Jones, Ohnacker, Neal), the otitis followed upon scarlet fever; in two instances (Netter, Crockett) following measles. In Lang's case the scarlet fever was questionable, but an acute tonsilitis was present. One case followed upon brain abscess (Day); one after submucous nasal septum resection (Graef and Wynkoop); three occurred after trauma to the

Head (Dandy, Leighton and Pringle, McCarthy); one after trauma to the back (Barth); two were questionable in origin, the first (Patzig) having played football the previous evening, the second developing otitis media after the onset of the meningitis (Urbantschitch). Two cases followed upon acute tonsillitis alone (Vining and Thompson, Rosenberg and Nottley); one occurred after removal of a cerebellopontine tumor (Dandy). In two instances (Tedesco, Weaver) no source of infection could be demonstrated.

Organism: In some of the early cases the diagnosis rested on finding streptococci in the smear of the turbid spinal fluid, no culture being reported. These observations cannot have the finality that isolation of the organism on culture media necessarily imparts. Yet streptococci are so rare as contaminating organisms, that their presence in the smear alone is sufficient evidence, it would seem, to stamp the case as of streptococcic origin. In one instance (Schenke and Streit) only one organism was found in the smear.

The classification of organisms found is as follows:

Streptococcus (type not specified)	21
Streptococcus hemolyticus	10
Streptococcus hemolyticus (scarlet fever group)	1
Streptococcus pyogenes	4
Streptococcus viridans	4
Streptococcus mucosus	1

Treatment: Only a casual study of the cases gathered here will suffice to disclose the varied method of treatment employed and to emphasize that no successful specific procedure has yet been evolved.

In seven cases (Patzig, Netter, Schulze, Tedesco, Neal, Shaw, Acker) lumbar puncture alone was successful, and in one instance (Bowers) lumbar puncture and jugular ligation. Huenekens and Stoesser did a mastoidectomy and employed irrigation of the spinal canal with normal saline. McCarthy injected human serum intraspinally. Mastoidectomy and repeated lumbar puncture were successful in three cases (Bondy twice, Schenke and Streit). Watson-Williams employed intraspinal injections of a silver preparation (collosol argentum) after doing a mastoidectomy. In six instances mastoidectomy alone proved sufficient (Alexander, Askey, Scott, Mygind, Yerger and Voss), and in one instance labyrinthotomy (Bondy). Lumbar laminectomy and drainage were done in three cases that recovered, once by Barth and twice by Leighton and Pringle. McKenzie drained the spinal fluid by way of a wire drain in the internal ear and an incision in the cerebral dura. Alexander performed labyrinthotomy and drained cerebro-spinal fluid through the dura and also locally by way of the internal ear. Dandy on two occasions instituted surgical drainage through the cisterna magna, and Day drained the cerebral dura alone. Graef and Wynkoop were successful with autogenous streptococcus vaccine subcutaneously. Antistreptococcus serum was used either alone or in conjunction with other methods by Weaver, who gave antistreptococcus serum intraspinally; by Crockett and DuBois and Neal, who used antistreptococcus serum intraspinally and urotropin by

mouth; by Ohnacker, who performed mastoidectomy and made use of antistreptococcus serum intraspinally; by Urbantschitch, who followed Ohnacker's procedure, but also used urotropin intravenously; by Vining and Thompson, who employed antimeningococcus and antistreptococcus serum intraspinally; by Day, who gave antistreptococcus serum intraspinally and autogenous streptococcus vaccine subcutaneously; by Neal and Jones who used anti-scarlet serum intraspinally and, on one occasion, 3-4 cc. of 1 per cent neutral acriflavine. On another occasion Neal used antibacterial and antitoxic serum (scarlet), prepared by the New York Department of Health, intraspinally and 5000 units once intravenously. Lang was successful using antimeningococcus serum at first and then antiscarlet serum intraspinally and intravenously. He also resorted to two blood transfusions. In our own case, antimeningococcus and antistreptococcus serum was used intraspinally, the latter in conjunction with irrigation of the canal with 1-4000 solution of neutral acriflavine.

Comment: Surely, when in forty-one definite cases of recovery so many different procedures are resorted to, it is not necessary to call attention to the absence of a specific treatment for streptococcus meningitis. To suggest that many of these cures are spontaneous and would have occurred regardless of treatment or sometimes in spite of it, would not be at all original. Dandy, discussing his own cured cases, says, "although the mortality is extremely high, spontaneous cures do occur, a fact which makes it open to doubt whether many recoveries—including my own—have not really occurred in spite of, rather than because of, treatment. Indeed some forms of therapy are so vigorous and many so devoid of surgical and physiological reasoning that one is forced to the conclusion that actual damage has been added to very sensitive tissues which need all their strength to combat the infection."

Brieger produced experimental streptococcus meningitis in dogs and noted spontaneous recovery in four of fourteen cases which were untreated. Recovery also was spontaneous in one of three untreated cases in monkeys.

In the light of our own case and in the attempt to evolve a logical method of treatment, it is of more than usual interest to note the result of animal experimentation carried out by Kolmer, Rule and Madden. These authors have been successful in treating induced streptococcus meningitis in dogs with chemotherapy and serum therapy, employing antistreptococcus serum and gentian violet or neutral acriflavine by cerebral cisterna lumbar lavage. They noted the following: "Furthermore, there is no chemotherapeutic agent for streptococcus infections comparable to ethyl hydrocuprein hydrochloride for pneumococcus infections, although I believe that the addition of gentian violet or neutral acriflavine to antistreptococcus serum appreciably enhances its streptococcidal activities." These writers have as yet had no success in human cases, but they add further: "A polyvalent antistreptococcus serum, therefore, should be employed and to each 25 cc. one may add 1 cc. of a 1: 100 solution of gentian vio-

let or acriflavine in sterile physiologic solution of sodium chloride. The mixture should be warmed before injection, or a 0.5 per cent solution of neutral acriflavine may be employed."

Enough successful work with acriflavine solution and antistreptococcus serum has, of course, not yet been reported. It would be presumptuous for us even to attempt to detail any method of treatment as having a greater likelihood of cure than another. Yet, on the basis of experimental data and of the successful outcome in our own case which seemed so nearly hopeless, we would like to see our method tried in other cases.

The routine resort to surgical interference and the expressed opinion that suppurative meningitis is as much a surgical condition as is suppurative peritonitis, we do not believe to be sound. Surgical removal of any offending focus, particularly in connection with demonstrated ear infection, should, on the other hand, by all means be done.

Should routine mastoidectomy be done in cases of streptococcus meningitis, even though the ear drums appear normal? Urbantschitch did this in his own case and advocates it as a necessary procedure in treatment of streptococcus mucosus meningitis, regardless of the normal appearance of the tympanic membrane. That this may apply in cases of streptococcus mucosus meningitis is possible. We do not believe it applicable to streptococcus meningitis in general. We cannot agree, too, that the early mastoidectomy in Urbantschitch's case was directly responsible for the recovery. The bilateral mastoid operation was done on January 8th; yet the patient continued to have bouts of remittent fever and meningeal signs through the months of January, February, March, and part of April. In our own case of undemonstrable origin, we cannot see how mastoidectomy in the presence of normal drum membranes, which remained so throughout the course of the disease, could have served any useful purpose. On the other hand, it may have been productive of much harm.

The procedure of cerebellar decompression and drainage of the cisterna magna was employed in suppurative meningitis, but unsuccessfully in six cases by Haynes and Kopetzky. Day failed to get a cure with this procedure in nine cases. The latter author says that, though drainage of the cisterna magna hinders the development of a diffuse meningitis over the hemispheres and prevents the accumulation of pus in the pia arachnoid, it does not influence the progress of the infection at the base of the brain. It appears to have no effect on the accumulation of inflammatory exudate in the subdural spaces. Neal says that the results of operative procedures in general have been very discouraging.

Indefinite Cases Not Included in the Series

For the sake of completeness, some indefinite cases not included in the group of recovered cases because of incomplete data or complicating factors must here be described.

Gleich reported a case in a male colored infant, aged two months, who developed a streptococcus meningitis and was treated by antimeningococcus and antiscarlatinal serum. Improvement followed. Yet, two and one-half months after the onset, streptococci were still demonstrable in the spinal fluid. Hydrocephalus developed and the infant, who never left the hospital, died at the age of seven months from broncho-pneumonia.

In Bryant's case the data are meagre. His patient was a man 22 years old with definite meningeal signs and in whom recovery ensued after decompression and mastoidectomy. No mention is made whether the organism was diagnosed on smear or culture, and the patient died after 188 days "from toxemia caused by repeated secondary infection of the decompression wound."

Gruening, discussing a paper before the New York Otological Society in 1904, "remembered a case of a boy whom he had operated on for brain abscess some five years ago. He was taken very ill with convulsions and stupor, with the discharge of a serous fluid from his ear. Lumbar puncture was performed and the fluid evacuated was distinctly turbid and contained streptococci. The case recovered." No other details are given.

In Rainey and Alford's case the culture of streptococci was made from spinal fluid discharging through the ear and not from fluid removed directly from the cerebro-spinal system. Brieger mentions two cases of recovery in streptococcus meningitis in which the organism was demonstrated in smears of the cerebro-spinal fluid, and Denker also reports, without detailed description, a case of recovery from streptococcus meningitis. The organism was isolated on culture and demonstrated also on direct smear.

Bacteria in the Cerebro-spinal Fluid Without Meningitis?

In considering cases of recovery from purulent meningitis, it is well to consider for a moment that cases are recorded in the literature that showed organisms in the spinal fluid and yet revealed no meningeal involvement at autopsy. Heubner reported two cases in children with thrombosis of the longitudinal sinus, the first complicating otitis, the second following upon a widespread eczema. A pneumococcus in the first case was isolated from the blood-tinged spinal fluid and from the thrombus itself. In the second case a streptococcus was isolated also from slightly blood-tinged spinal fluid and from the removed thrombus. In both cases there were no signs of meningeal involvement demonstrable at autopsy. Voss also observed on three occasions the presence of organisms in the spinal fluid without the slightest sign of meningeal involvement, twice with sinus thrombosis, and once with sepsis of otogenic origin without thrombosis. Voss states that in one-fourth of his cases of sinus thrombosis, bacteria were present in the spinal fluid without complicating meningitis being evident. In two cases organisms were present in the spinal fluid when no sinus thrombosis was present, yet with no meningitis at autopsy.

Are these instances of very early cases which would have developed meningitis had they lived longer? There are those who favor this hypothesis

(Pfaundler and Gerhardt), the latter of whom quotes a similar expression of opinion by Lesnee. Others believe (Voss) that the presence of organisms in the spinal fluid is not always indicative of early or threatened meningitis, but may be found when organisms are present in the blood stream—a sort of seepage by way of the choroid plexus. According to the latter author, the virulence of the organism is an important factor and may be lessened by such passage from the blood stream.

To us such a discussion appears to have only academic interest. It cannot alter the fact that a turbid spinal fluid which contains pyogenic organisms determines the presence of a purulent meningitis. It is perhaps possible that non-active but living organisms may be demonstrable in a clear spinal fluid and yet no meningitis be present, but when the cerebro-spinal fluid is turbid and not contaminated by blood and contains organisms, then a true meningitis must be diagnosed.

Localized versus Diffuse Suppurative Meningitis

Writers have long pondered over this subject of localized and diffuse purulent meningitis, some contending that only in localized cases is recovery possible. The German literature particularly often goes into a long discussion of the problem. That we are on controversial ground in a question of this nature is not to be disputed. There is no way of differentiating clinically between the two types, although some authors have attempted to do so by comparison of the severity of symptoms. We do not believe that this can be done with sufficient accuracy to arrive at any clinically helpful or trustworthy conclusions drawn from such observations.

Whiting, from a large experience, says: "I have always said, namely, that our cases of general suppurative meningitis all die." Alexander, on the other hand, stresses the impossibility of clinically differentiating diffuse from localized meningitis and believes that his case of recovery was one of a diffuse purulent type. Only ultimate autopsy in recovered cases might help solve this problem. Day's case, which came to necropsy two years after a streptococcus meningitis, showed what appeared to be only a localized area of adhesions cementing down the membrane and obliterating a limited area of arachnoid space. That these findings prove beyond possible doubt the localized nature of the meningitis, we do not believe to be true. It is possible that the drainage strands may have caused sufficient traumatic inflammation to produce adhesions in the area thus injured.

Summary

There is as yet no specific therapy for streptococcus meningitis. With the development of antistreptococcus serum in recent years, however, the rational procedure would appear to be the use of this serum intraspinally, coupled with the effort to eliminate any demonstrable source of infection, particularly of otitic origin. Of interest will be a further study of the value of irrigating the spinal canal with dyes, such as neutral acriflavine, in conjunction with other indicated treatment. The possible value of such a procedure is suggested by our own case and

by the experimental work of Kolmer and his coworkers. The possibility of spontaneous recovery from this disease must be kept in mind in attempting to evaluate any therapeutic measures.

Conclusions

1. A case of streptococcus hemolyticus meningitis with recovery is reported.

2. Forty additional cases of meningitis due to the streptococcus have been collected from the literature and analyzed. The method of treatment upon which recovery followed is indicated in each case.

ANALYSIS OF REPORTED CASES

Author	Sex	Age	Treatment	Organism	Remarks
Schenke and Streit 1901	M	35	Mastoidectomy	Streptococcus (Type not specified) Only one organism seen on smear.	A 35 year old machinist with an ear discharge since November 1899 was admitted April 27th, 1900 complaining of severe headache, dizziness and vomiting. There was tenderness over the left mastoid and along the spine and pain on moving the head. There was a discharge from the left ear. Temperature moderate. He was operated on April 28th and mastoidectomy revealed sclerosis of the bone and pus in the mastoid cells. The antrum mucosa was of dirty greenish color. The spinal fluid was slightly cloudy, the smear of which showed no collection of leucocytes but in one preparation a single short chain streptcoccus was seen. The culture of this fluid was unfortunately not further studied. On three other occasions the culture of the spinal fluid was sterile. The patient was discharged May 12th, still having some left hemicrania and a discharging ear. In November 1900 he was well except that strenuous work produced headache. In July 1901, there was a return of discharge from the left ear.
Walter Schulze 1903	12	M	Lumbar Puncture	Streptococcus (Type not specified)	Patient a boy aged 12 admitted September 3, 1902. History of suppurative otitis in early childhood which never gave trouble again until July 1902. Ear discharged from July until he came to hospital. Rather drowsy on admission, vomited at times, hyperaesthetic, pain on pressure over cervical spine, marked tenderness behind right ear. Developed left facial paresis, continued to vomit. Temperature up to 102 F. September 4th: Patient stuporous, herpes labialis is present. Lumbar puncture—fluid cloudy, under increased pressure, about 25

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					cc. removed. Leucocytes present. On a smear stained 40 minutes a short chain streptococcus and a few diplococci were seen, "which were apparently also streptococci." Still complained of headache, marked stiffness of neck. Pupils unequal. Until September 16th: Ran an irregular temperature but seemed somewhat improved, then developed edema and tenderness behind right ear. Lumbar puncture water clear but without bacteria. Operation revealed subperiosteal abscess, large deeper abscess was also opened, the sigmoid and transverse sinus were exposed. The former was yellowish white in its upper portion, between the sinus and the overhanging bone the dura was loosened anteriorly and above; the extradural abscess extended into the middle cranial fossa. No blood flowed from the incised sinus. A grayish black thrombus was present. September 19th, improved. Purulent discharge continued from ear. Temperature normal. September 28th: Wound granulating. October 3rd: Ear dry and on October 13 wound healed and patient discharged. It will be noted that the spinal fluid prior to operation had become clear and the author notes his belief that healing of the meningitis had already occurred before the procedure of operation was undertaken.
Voss 1905	7	F	Mastoidectomy	Streptococcus (Type not specified)	The data in this case is meagre. Patient was a blind girl aged 7 in whom recovery followed otitic meningitis. The condition occurred as a complication of scarlet fever and mastoiditis. Mastoidectomy was done. The spinal fluid was blood tinged and stood four hours before it was smeared and stained. The smear showed gram positive diplococci and short chained streptococci. A few lymphocytes were present.
Alexander, G 1908	10	M	Operative incision of semi circular canals opening of vestibule and cochlea. Incision of the dura. Lumbar puncture.	Streptococcus in spinal fluid. (Type not specified) and B. coli from the abscess.	Chronic suppurative otitis media left. Purulent labyrinthitis with fistula. Extra dural abscess. Suppurative pachymeningitis. Discharging right ear for four years. In December 1906 operative procedure was done at home with little relief. July 19, 1907 operation through old wound as described in

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					treatment. Cholesteatoma found. Post operative course of moderate severity. Troublesome nystagmus; discharged, however, on July 26 improved and with good equilibration.
Alexander, G. 1908		24 M	Radical Mastoidectomy	Streptococcus (Type not specified)	Since childhood patient suffered from discharging ear. Treated for cardiac condition for past seven weeks. Has again been troubled with ears and has headache, occasional dizzy spells and periods of blackness before his eyes accompanied by vomiting. Stiff neck present. Left ear discharging foul pus. Right drum slightly altered. October 21st, 1907: Operation done, cholesteatoma found. Posterior and middle fossa exposed as well as the sinus. Dura incised with the liberation of cloudy cerebro spinal fluid. Lumbar puncture gave cloudy spinal fluid. Gram positive cocci in diplo and strep formation found. October 30th: Temperature normal. November 23rd: Completely recovered.
Netter, A. 1909	7	F	Lumbar puncture only	Streptococcus (Type not specified)	Meningitis complicating double otitis media after measles. Two punctures were done July 23—July 27, 1900. Recovery complete.
Mygind, H. 1910	13	M	Radical Mastoidectomy	Streptococcus pyogenes	Boy 13 years old with a history of right sided purulent discharge since age of 10, following scarlet fever. 4 days prior to admission severe pain in right ear. Doctor removed polyp from right ear. This was soon followed by dizziness and vomiting. On examination an exostosis was present deep in the right ear canal and the remnant of a removed polyp visible. No drainage. Slight Kernig sign. No stiff neck. Spinal fluid cloudy under greatly increased pressure, containing polynuclears and a few gram positive diplococci very much like streptococci. Unquestionable streptococci were later cultured from the pus of the perisinus abscess. These cultured as streptococcus pyogenes on agar. Day after admission radical mastoidectomy right side. The mastoid process was filled with dark granulating masses of foul pus, an abscess was found with a fresh

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					thrombus in the lower portion of the sigmoid sinus, the lateral wall of which was resected. Dura was normal. After the operation pain on bending head, and a positive Kernig sign were present for a time. After 14 days patient up and about.
Graef, C and Wynkoop,, R. B. 1910	24	F	Autogenous Streptococcus vaccine	Streptococcus (Type not specified)	March 20, 1910: Submucous resection of nasal septum under cocaine anaesthesia. Vomited several times next day. On 2nd day postoperative developed headache with sudden rise in temperature to 104 F. Pain in spine and nape of neck. Marked convergent strabismus and delirium on following day. On March 27th, cloudy fluid obtained on spinal puncture, culturally sterile but on smear gram negative cocci arranged in pairs. March 30th a second spinal puncture gave cloudy fluid which showed streptococci on culture. Patient in low muttering delirium. April 2nd was given autogenous vaccine 10 million organisms and a similar dose daily for five days. The dosage was then increased 3 million a day until 25 million was reached. This level was kept for five days and the vaccine then given twice a week. The patient was discharged cured 38 days after admission to hospital.
Ohnacker, Paul 1911	5	F	Mastoidectomy Anti streptococcus serum intraspinally	Streptococcus (Type not specified)	Girl age 5—admitted February 15 with severe scarlet fever. Temperature subsided in few days. February 21st and 25th redness was noted, drum ruptured spontaneously and temperature subsided. February 27th—Temperature again elevated, drum incised, no relief. Stiff neck and Kernig present. Mastoidectomy was done and pus found in antrum. The lateral sinus was involved and hence freely exposed. Puncture liberated a chocolate colored fluid mixed with pus particles, the thrombus present was removed till free bleeding occurred. Culture of granulations found at operation gave a long chain streptococcus. Lumbar puncture next day gave a clear sterile fluid. After a week the temperature and symptoms subsided only to rise again March 10th. Left ear drum now involved and mastoidectomy done. After a few days of improvement, again symp-

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					toms of meningitis. Repeated lumbar puncture, though sterile, contained numerous leucocytes. Two injections of 20 cc. of antistreptococcus serum were given intraspinally. Radical mastoidectomy was done. Through a defect in the dura from which spinal fluid oozed in large amounts, a puncture was made, yielding cloudy serous fluid mixed with blood from which streptococci were cultured. After several sequestra were discharged, healing occurred, recovery took place and patient was up June 15th.
Tedesco, Fritz 1911	20	F	Repeated Lumbar Puncture	Streptococcus (Type not specified)	Sudden onset with headache, vomiting, fever April 12, 1911. Bluish spots on body developed but these disappeared in two days. Admitted 4/16/11—with stiffness of neck and bilateral Kernig, optic neuritis present. 25 cc of cloudy fluid under increased pressure removed, temperature 102.5. 4/19/11 lumbar puncture repeated and again on 4/28/11. Made gradual recovery and was up May 9th, 1911.
Day, E. W.	Not giv'n	Not giv'n	Dural Drainage. Twisted strands of cat gut inserted between dura and brain tissue.	Streptococcus (Type not specified)	Four days after evacuation of temporosphenoidal abscess, symptoms of meningitis with turbid spinal fluid. Convalescence uneventful. Discharged after several weeks. Re-admitted two years later with recurrence of abscess in the old cavity, and died from rupture of an undrained pus pocket into the lateral ventricle. Note: One half hour after death a canula was introduced into the posterior horn of the lateral ventricle and an exit given by a needle in the lumbar spinal canal. A methylene blue solution introduced above appeared in fast drops at the lumbar needle. At autopsy the subdural arachnoid was stained blue, except for an elliptical area four inches by two inches on the outer and under surface of the temporal and cerebellar lobes of the left side, into which the staining solution had not penetrated. The membranes were here cemented together, and the arachnoid spaces destroyed. This clear area corresponded to the center of the region in which the dural drains were used two years before. The writer suggests the possibility that in re-

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					covered cases the lesion is anatomically localized, though clinically giving symptoms of diffuse meningitis.
Day, E. W. 1913	19	F	Anti streptococcus serum intraspinally. Autogenous streptococcus vaccine subcutaneously	Streptococcus (Type not specified)	Operated on December 6th, 1908 for a simple mastoiditis. 15 days later evidence of diffuse suppurative meningitis. After 48 hours 10 cc. of anti streptococcus serum intraspinally and 12 hours later 100,000,000 dead streptococcus (autogenous) vaccine was given subcutaneously. Both injections were repeated in 48 hours, on the 5th day spinal fluid less turbid. Temperature normal on 8th day. Several additional subcutaneous vaccine injections were given during convalescence. Well when seen 4½ years later.
Barth 1914	19	F	Lumbar Laminectomy and drainage.	Streptococcus (Type not specified)	15 days after an injury to her back incurred Dec. 25th developed headache and vomiting, and 5 days later admitted to the hospital. Turbid spinal fluid at first showed no organisms. On January 29th streptococci were isolated from the spinal fluid. January 31st lumbar puncture, laminectomy and drainage (3rd and 4th lumbar) were done. After a stormy course gradually improved. February 20th the drain was removed. Toward end of March patient out of bed and apparently recovered. This author believes that streptococcus meningitis is a surgical disease, just as acute peritonitis is surgical.
Leighton and Pringle 1915	8	F	Lumbar Laminectomy and drainage	Streptococcus (Type not specified)	5 weeks before onset sore throat, 3 weeks before onset otitis media and swelling behind ear. Admitted December 16th, 1914 and condition diagnosed as mastoiditis. 3 days later typical meningeal symptoms. On lumbar puncture bloody fluid obtained. Under ether anesthesia December 19th, 1914 lumbar laminectomy (3rd and 4th lumbar) done. Post operative course stormy, but improvement progressive. Temperature normal January 4th, 1915. Discharged February 6th, 1915.
Du Bois P. L. and Neal, J. B. 1915	26	M	Antistreptococcus serum intravenously and intraspinally and streptococcus vaccine subcutaneously.	Streptococcus pyogenes	Onset 8 days after incised ear drum for otitis media; anti-streptococcus serum was given intraspinally and intravenously and also streptococcus vaccine subcutaneously. On the 6th day difficulty in obtaining fluid was encountered and the taps stopped. Urotropin

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			Urotropin up to 120 grains per day		was given from the onset 30 grains per day and then up to 120 grains per day. Slight tremulousness and pain in back and extremities developed and except for impaired sensation and weakness, pain cleared with salicylates.
McKenzie, Dan 1915	50	M	Surgical procedure. Incision and drainage of spinal fluid through dura.	Streptococcus (Type not specified)	Left mastoidectomy in September 1914. October 22, 1914, radical mastoidectomy was done on both sides. An eroded bony sequestrum removed on right side, October 25th—Headache, fever, irritability. October 28th—stiff neck—20 cc. of spinal fluid from which streptococci were cultured. Operation—dura on right side incised, liberating free flow of spinal fluid. Wire drain in internal auditory meatus. No lateral sinus disease. Gradually improved. Temperature normal November 18th.
Leighton and Pringle	65	M	Lumbar Laminectomy and drainage.	Streptococcus (Type not specified)	Onset three weeks after injury to head which knocked him unconscious for a few minutes. Lumbar laminectomy under spinal anesthesia. Loss of sphincter control for nine days. Regained consciousness after two days. Drain removed on 5th day, gradual recovery. Slight meningocele developed.
Crockett, E. A. 1916	16	M	Lumbar puncture antistreptococcus serum.	Streptococcus (Type not specified)	Double otitis media following measles. 4 days later mastoidectomy, bilateral, done, with complete healing in 12 days. 3rd day post operative became comatose. Questionable stiff neck and double Kernig. Temperature 104. Lumbar puncture clear but on centrifugation streptococci found on smear. 2 days later convulsions followed by right facial paralysis and weakness on right side of body lasting two days. Streptococcus serum given intravenously on 1-2 occasions. Urotropin by mouth. Made gradual recovery.
Bondy 1917	M	21	Radical Mastoidectomy	Streptococcus pyogenes	Admitted October 25, 1915 in semicoma. History difficult to elicit, answers questions when aroused and goes off to sleep again. Vomiting and fever for 12 days prior to admission. For 6 months ear trouble on right side. Marked stiffness of neck. Positive Kernig. Temperature 104 F. Left ear normal. Right ear discharging a fetid pus.

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					December 27th: Mastoid opened and found sclerosed. Pus and broken cholesteatoma in mastoid and antrum. Radical operation done, dura exposed in the middle fossa and extra dural abscess found. The dura was covered by greenish exudate. Exposure carried till healthy dura found but medially this was not possible. The dura was slit and an iodoform wick placed in the sub dural space. Lumbar puncture yielded cloudy fluid under markedly increased pressure, containing streptococcus pyogenes. October 28th: Temperature about 102. Slightly clearer mentally. October 29th: Temperature practically normal but complaining of headache. Epileptiform seizure of Jacksonian type at noon. October 31st: Two epileptiform seizures. November 2nd: Spinal fluid clear. November 3rd: Patient again comatose. Temperature 100. Marked stiff neck, Kernig and stertorous breathing. November 10th: Gradually improved. Lumbar puncture clear and sterile. November 18th: Up a little while. November 26th: Neurological examination negative except for sensitiveness over vertebrae. January 31st: Discharged home.
Bondy 1917	43	M	Labyrinthine Operation	Diplostreptococci	Admitted April 7, 1915. Since childhood purulent infection and difficulty in hearing—both ears. April 8th: Radical right mastoidectomy. Mastoid sclerosed, cholesteatoma present. April 15th: Up and about. May 17th: In an attempt to remove polypi, which had formed, by means of a wire snare the wire broke and the instrument was pressed in. There was prolonged nystagmus and dizziness but the patient managed to go home alone.

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					May 18th: Vomiting and dizziness set in abruptly. He returned to the clinic complaining of vomiting and severe headache. Nystagmus was present toward the healthy side. May 19th: Stiff neck, right positive Kernig sign, severe headache. Temperature 102.2 F. Labyrinthine operation, vestibule opened, exposed dura normal. Lumbar puncture showed cloudy fluid containing diplo—streptococci. May 20th: Temperature normal though meningeal signs and nystagmus less. Kernig still present. May 31st: No nystagmus, meningeal signs have entirely cleared up. July 12th: Discharged from the hospital. Wound clean, no complaints except for occasional dizziness.
Bondy 1917	28	M	Lumbar Puncture	Streptococcus pyogenes	Admitted March 27th, 1916 complaining of severe headache for the past ten days. On February 24 was operated on at a military hospital for acute right mastoiditis and wound has been draining since. Operated on April 1st, by incision through old scar, granulations removed, and exploration continued until dura of the middle fossa and the sinus were exposed. Headache persisted after operation and temperature remained elevated. April 21st: Severe headache: Unable to sleep at night. Some visionary disturbance. Right 6th nerve weakness, again operated upon, wound cleaned and granulations removed. Probing in several directions yielded nothing. Lumbar puncture slightly turbid but under normal pressure contained streptococci. April 26th: Lumbar puncture blood tinged, containing streptococcus pyogenes. May 4th; Lumbar puncture sterile. July 4th: Recovery complete, wound healed. Temperature subsided in 12 days but abducens paralysis did not clear completely for 8 weeks. Discharged home.

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Weaver, G. H. 1919	25	F	Antistreptococcus serum.	Streptococcus viridans	Onset September 23: Temperature normal on October 12 and stayed normal till October 17th, then exacerbation of meningeal symptoms, treatment continued, reached normal October 23rd. "The improvement that followed each administration of anti-streptococcus serum was striking."
Watson-Williams 1920	37	M	Silver preparation (collosol argentum) intraspinally.	Streptococcus (Type not specified)	Admitted September 23, 1919 with pain in the left ear and dizziness. Purulent discharge from left ear since boyhood. September 25th: Headache, vertigo, spontaneous nystagmus to left. September 26th: Lumbar puncture turbid. Mastoidectomy and labryinthotomy was done. September 28th: Lumbar puncture. October 2nd: Somewhat improved. October 6th: Severe headache again, lumbar puncture done, 15 cc. of cloudy fluid removed and 1 cc. of collosol argentum injected. Streptococci were cultured from spinal fluid. October 7th: 3 cc. of collosol argentum intravenously. Spinal fluid still turbid. October 8-19th: Daily lumbar puncture preceded by 3-5 cc. of collosol argentum intravenously. Made a gradual but complete recovery.
J. B. Neal, 1921	5	F	Lumbar Puncture	Streptococcus hemolyticus	Onset following otitis media. Slight stiffness of neck, headache, irregular temperature up to 105. Spinal fluid had a practically normal sugar content. The author believes this to be a case of localized meningitis. No intraspinal injections were given only lumbar puncture being resorted to. Recovery ensued.
Shaw, Henry 1921	8	M	Lumbar Puncture	Streptococcus hemolyticus	Left ear incised October 24th followed by good drainage. Developed headache which continued. On November 10th left squint noted. November 15th: Temperature rose to 104, marked hyperaesthesia was present. Spinal puncture gave a clear fluid containing only 18 cells. For two days there was slight improvement but on the third day meningeal symptoms were again in evidence and the temperature rose. Lumbar puncture now

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					gave cloudy fluid under pressure which gave a pure growth of streptococcus hemolyticus. With remissions from time to time relieved greatly by lumbar puncture, recovery gradually ensued. Discharged home January 14th two months after admission.
Acker G. N. 1921	12	M	Lumbar Puncture	Streptococcus hemolyticus	Onset January 14th, 1921 with pains in the right ear and moderate temperature. January 22nd: Temperature 104, headache and vomiting. January 28th: Stiff neck and Kernig. January 29th—Lumbar puncture fluid was cloudy and contained streptococcus hemolyticus on culture. January 31st: Puncture repeated. Ran a fairly severe course, delirious at times; had several nose bleeds. About February 15th began to improve and made uneventful recovery. In discussing this case Dr. Heiman said: "I should like to add another case occurring in a girl 7 years old, seen three months ago. Lumbar puncture yielded a turbid fluid. All signs of meningitis were present. The treatment was symptomatic. No vaccines were used. The streptococcus hemolyticus was found. The child made a perfect recovery."
Scott, Sidney 1921	10	F	Radical Mastoidectomy	Streptococcus (Type not specified)	Admitted July 23, 1920 with purulent discharge from left ear, unconscious, temperature 104, stiff neck and Kernig present, marked rotary nystagmus to the right. A radical mastoidectomy was done, cochlea was extirpated and translabyrinthine drainage was established. 10 cc. of cloudy fluid removed on lumbar puncture containing streptococci. Puncture was repeated at intervals of twelve hours during next few days. On 4th day spinal fluid was clear and sterile. Despite temporary facial paralysis, recovery was uninterrupted.
Patzig, D. 1922			Lumbar Puncture	Streptococcus viridans	Onset in the morning of June 25th following a football game the evening previous. Next day he had a chill, fever vomiting and rise in temperature. Severe headache, pain in the back of neck and back generally. On admission, stiff neck and positive Kernig. June 27th

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					lumbar puncture under increased pressure, cloudy, from which streptococcus viridans was cultured. June 30th: Temperature normal, meningeal symptoms had disappeared. July 16th: 1921—Discharged—Cured.
Bowers W. C. 1922	34	M	Lumbar Puncture Jugular Ligation	Streptococcus hemolyticus	Patient had discharging ear for 15 months and mastoidectomy was done. Day after operation developed headache, stiff neck, positive Kernig; hemolytic streptococci were cultured from the spinal fluid. On 19th day blood culture was positive for hemolytic streptococci. On 20th day jugular ligation was done. After 12th day meningeal signs cleared up but local and general condition persisted. Was discharged well 61 days after mastoidectomy.
Yerger, C. P. 1922	40	F	Removal of focus in ear by mastoid operation.	Streptococcus (Type not specified)	Onset one week after operation for otitis media of ten days duration following measles. Simple mastoidectomy on day of admission. 2nd operation, exploration of cranial fossae. Well 39 days after admission.
Askey, Stephen 1923	12	M	Mastoidectomy	Streptococcus (Type not specified)	January 22, 1923 developed earache. Had considerable deafness of right side especially. Right ear drum thickened slightly. January 29th: Began to have pain right occipital region but no mastoid tenderness. February 3rd: Temperature 103.5. Stiff neck and Kernig sign present. Spinal fluid under reduced pressure, cloudy but gave a pure culture of streptococci. February 4th: Despite absence of signs of mastoid involvement, right mastoidectomy was done. A small area of diseased bone was found at the mastoid tip and pus in the mastoid cells. Temperature returned to normal in four days and boy made uneventful recovery.
Dandy, Walter 1924	6	M	Surgical drainage by way of cisterna magna.	Streptococcus hemolyticus	Following automobile injury boy bled from nose and left ear. Next day temperature 104.5, stiff neck and Kernig, spinal fluid had streptococcus hemolyticus. 36 hours after onset of meningeal signs cisterna magna was drained by a small rubber tube, tube removed on 7th day and wound drained spon-

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					taneously 2 days. 9 days post-operative, temperature normal. Recovery uneventful.
Dandy 1924	49	M	Surgical drainage by way of cisterna magna.	Streptococcus viridans	8 days after removal of cerebellopontine tumor rise of temperature, drowsiness, irrational. Spinal fluid showed streptococcus viridans. On 18th day surgical drainage of cisterna magna which continued 4 days. Then daily or twice a day punctures of lateral ventricle, spinal canal or of cerebellar cisterna, temperature still elevated 43 days after onset of drainage. Recovery ensued.
Vining and Thompson 1924	10	F	Antimeningococcus and antistreptococcus serum	Short chain streptococcus markedly hemolytic in character.	Two weeks following an acute tonsillitis which subsided spontaneously, developed meningeal signs, headache, stiff neck, positive Kernig. Lumbar puncture yielded 20 cc. of cloudy fluid. P-60%, L-40%. No organisms in direct smear. Next day after removal again of 20 cc., 15 cc. of antimeningococcus serum was given intraspinally and 10 cc. subcutaneously. Polymorphonuclears 64%—lymphocytes 36%. Fluid showed short chain streptococcus markedly hemolytic in character. Improvement on 2nd day following tap. 3rd tap on third day showed less turbidity. 10 cc. of antistreptococcus serum injected subcutaneously, 4th day distinct improvement, 5th day 6 cc. of clear fluid obtained.
Urbantschitch, E. 1926	21 mts	M	Lumbar puncture Anti-streptococcus serum Mastoidectomy Urotropin intravenously	Streptococcus mucosus	Admitted June 6th, 1926 with history of head cold and bronchitis. 8 days prior, child had poked a match in its left ear. Onset sudden January 4th with vomiting and fever. On admission no stiffness of neck, Kernig doubtful, ears normal. Lumbar puncture, not under pressure, a bloody tap from which streptococcus mucosus was cultured. On January 8th fluid under increased pressure. Despite essentially normal drums bilateral mastoidectomy done and pus found. January 9th: Lumbar puncture 2½cc. of antistreptococcus serum given. January 10th: Three attempts at lumbar puncture unsuccessful. January 14th: Lumbar puncture under fairly marked pressure, slightly cloudy, 3000 cells per cmm., continues to run an irregular course of temperature. January 21st: Spinal fluid still turbid but

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					sterile. Both ears discharging. January 28th: Still having evening temperature up to 103 or more. Lumbar puncture under greatly increased pressure and containing streptococcus mucosus. February 1st: Gravely ill, marked stiffness of neck. Kernig positive. February 2nd: 5 cc. of 40% urotropin intravenously. February 4th: Lumbar puncture unsuccessful. February 5th: Improved and continued to grow better despite occasional rises in temperature. Discharged home February 21st. Through March and April, draining ears and several bouts of fever. Ears ceased draining April 27th. He became entirely well. July 7th: Continues perfectly well.
Neal, J. B. and Jones, A. 1927	7	F	Anti scarlatinal serum of anti toxic and anti bacterial potency. On one occasion ¾ cc. of 1.% neutral acriflavine was added. At onset anti meningococcus serum was used.	Hemolytic streptococcus belonging to the "chief scarlet fever group"	Mild scarlet January 20, 1927 lasting two days, following which she was well. On the 5th day after onset, fever, headache and meningeal symptoms. Admitted on 10th day. Left suppurative otitis media present but no indication of mastoid involvement. Pyelitis was a complication; improvement began 2/14/27. Discharged 3/13/27 in excellent condition. "The high mortality of streptococcus meningitis is shown by the fact that this is only the 3rd case to recover among the 116 that have been seen by the meningitis division".
Huenekens E. J. Stoesser, A. V. 1927	7	F	Daily lumbar puncture, irrigation with normal saline.	Streptococcus hemolyticus	Onset following 2 days after incision bilateral otitis media. Bilateral mastoid operation was immediately done. 9th day post operative, improved. 16th day exacerbation; after 12 days treatment,, recovery. Mental condition normal three weeks after.
McCarthy, F. P. 1927	25	M	Daily lumbar puncture Normal human serum intraspinally.	Streptococcus viridans	Onset 2 months following severe injury to head, fever, chills and delirium. Improved on 8th day following treatment. Discharged after 1½ months. No sequela or complaints. Slight spasticity of legs at first, later cleared entirely.
Lang 1928	2	M	Antimeningococcus serum. Scarlatinal antitoxin intraspinously and intravenously (seven doses)	Streptococcus hemolyticus	A boy, aged 2, was admitted to the Babies hospital with a negative family history; he had never been sick before. He had been nursed for seven months. The present illness began abruptly five weeks before admission, with fever 104.5 F. and sore throat, which persisted. A diagnosis of scarlet fever without

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					a rash was made, and antitoxin was given. The child was sent to a hospital for contagion, where he stayed two days and was then sent home as "no case". Restlessness, constant crying, refusal of food and loss of weight were prominent symptoms during the first five weeks of illness. Two lumbar punctures and a blood culture gave negative results. Both ears were incised and discharged freely. Physical examination showed a well developed white, male child acutely ill, with a temperature of 102 F., and extreme irritability. The fontanel was closed and the neck rigid, right internal strabismus and Tache were present, and the Kernig and Brudzinski signs were positive. Lumbar puncture on admission showed cloudy fluid with 1,000 cells, 99% of which were polymorphonuclears. Globulin was present and sugar absent. Gram-positive cocci in chains were found in spreads made from the fluid, and cultures grew streptococcus hemolyticus. The urine showed a small amount of albumin, but was otherwise normal. Antimeningococcus serum was given at the onset, with a resulting rise in cell count. Scarlatinal antitoxin was then given intraspinously and intravenously (seven doses), causing a gradual rise at first in the spinal fluid cell count which then gradually diminished to 2,500. The spinal fluid sugar remained below 20 mg. The child was given two blood transfusions, and the spinal fluid cultures were positive for streptococcus hemolyticus on three different occasions. At present at the age of 4, he is well grown and well nourished, but mentally sub-normal. He still has attacks of irritability.
Neal, Josephine 1930	11	M	Combined antibacterial and antitoxic serum (scarlet) intraspinally and intramuscularly. Spinal puncture and cisterna puncture.	Hemolytic Streptococcus	Patient 11 years old, had an attack of scarlet fever on April 2nd, 1928. Two weeks later there was otitis media of the right ear. He began having meningeal symptoms on April 27th and was admitted on May 1st. He presented typical signs of meningitis, there was an internal strabismus of the left eye and double otitis media. The blood count was 5, 900, polymorphonu-

Author	Age	Sex	Treatment	Organism	Remarks
					clears 85%, Lymphocytes 15%. The blood culture was negative and the urine was normal. He received the combined anti-bacterial and anti-toxic serum (scarlet) prepared under the direction of the New York Board of Health, intraspinally on the third, fourth and fifth of May. He also received 5000 units intramuscularly on May 3rd. Two of the spinal fluids showed a hemolytic streptococcus which was also obtained from a cisterna puncture performed on May 18th, on which occasion no serum was given. He made a complete recovery and reported 1½ years later apparently well.
Author	Age	Sex	Treatment	Organism	Remarks
Rosenberg and Nottley 1931	6	F	Lumbar puncture Anti meningococcus and anti streptococcus serum and 1-4000 aqueous solution of neutral acriflavine intraspinally.	Streptococcus hemolyticus	Admitted February 23, 1929 with a history of acute tonsillitis six weeks previously. This was soon followed by backache, headache and vomiting. There was stiffness of neck, irritability and restlessness. Ears normal. Spinal tap gave turbid fluid under increased pressure. Prior to isolation of streptococcus anti meningococcus serum was given, then antistreptococcus serum. Failing to improve on this therapy neutral acriflavine 1-4000 aqueous solution was used to irrigate the spinal canal. Improvement was gradual but progressive and the child made a complete recovery.

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The Prognosis in Tuberculosis with Especial Reference to the Psychological Aspects

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MY PURPOSE, for the most part, in this discussion is to present some of the phases which have to do with the prognosis of pulmonary tuberculosis that come directly under the control of the physician and which I feel, in the majority of cases, determine the outcome.

It seems to me that, particularly in the past, as we have come in contact with pulmonary tuberculosis we have had a tendency to base our opinion regarding the prognosis largely upon the extent of the involvement or upon the feelings and appearance of the patient or perhaps more or less upon both of these taken together. Experience, however, has taught us that feelings and appearance are extremely deceptive and that, while the prognosis in general is better in the less extensive than in the more extensive cases, yet a certain percent of the early cases go on to a fatal termination while a certain less percent of the more advanced cases recover. Consequently, we have now come to realize that we must get away from giving an arbitrary opinion in any case and that we must regard the prognosis as rather an individual affair and that the outcome can be determined only as we follow the case along.

However, about the first thing those of us who are handling tuberculosis patients are called upon to do is to give an opinion as to the outcome, and this demand is repeated from time to time during the course of the disease. In order, then, to satisfy not only our own minds to a certain extent, but particularly to satisfy our patient and, in many cases, his relatives, we must formulate some idea about the prognosis.

Having had an opportunity to carefully study and observe a case over a period of a month or more, it is possible perhaps to have some idea of the outcome through a proper evaluation of the important symptoms and, to a less extent, by the evaluation of the indication of the physical signs. As Lawrason Brown has said, it is the symptoms which tell us what is going on at any particular time. Consequently, as, in a general way, the symptoms increase or decrease, the prognosis is unfavorable or favorable. Dr. Brown says also that the physical signs tell us what has taken place in the past. But periodic physical and x-ray examinations, as they may indicate an increase or decrease in the physical signs and the extent of the involvement, will give us some definite information as to the progression or retrogression of the disease. In forming these general ideas about the outcome we should bear in mind that the course of the disease may change from month to month and with

it the symptoms and physical signs, so that our opinion regarding the prognosis may change accordingly.

We should also remember that since there are so many different factors which influence the course that a case of pulmonary tuberculosis pursues and since so many of these factors are dependent upon the individual element, we never see two people who have tuberculosis alike any more than we see two people who look alike, act alike, or talk alike. Dogmatism, then, in the prognosis of tuberculosis is not possible.

In general we should keep in mind that today tuberculosis is regarded as the most curable of chronic diseases; that active pulmonary tuberculosis, regardless of the extent, is always serious, at least until the physician and the patient regard it seriously. Again, we should remember that pulmonary tuberculosis is cured by attention to details; that a certain few patients with pulmonary tuberculosis, although they disregard details, get well in spite of what they do rather than because of what they do; but that for everyone who gets well under these conditions perhaps from forty to fifty people that ought to get well under proper circumstances lose their lives because, through their own neglect or through outside influence or advice, they have disregarded the details of the cure. We hear little of the story of these people who die, however, because dead men tell no tales.

As I have said, the prognosis in tuberculosis is, at best, uncertain because it depends upon so many different factors, such as age, sex, habits, and opportunity to take the cure, which are more or less fixed, while others, such as the virulency of the infecting bacilli and the resistance of the one infected not only differ in each case of pulmonary tuberculosis, but are changeable and are greatly modified by the way in which the patient adjusts himself to the cure and by the way he reacts to the cure.

In other words, at the beginning of each case of pulmonary tuberculosis we can conceive of a certain virulency of the infecting bacilli and a certain resistance of the host. The ultimate outcome of the contest waged between these two antagonists is what determines whether the patient lives or dies. The contest, however, during the course of the disease, is influenced by many factors which tend to increase or decrease the resistance of the host and at the same time decrease or increase the power of the bacilli to grow and produce destruction. The factors which have the greatest bearing upon the outcome of this contest in most cases are the psychological reactions of the patient while he is endeavoring to take the cure, and it is to these that I want particularly to call your attention. Today it is generally conceded that from eighty to ninety percent of the influences which determine the prognosis are psychological and have to do with the emotional, mental and nervous reactions of the patient.

I have referred in a general way to some of the factors which influence the prognosis in tuberculosis over which the physician has little, if any, direct control. It is true that in a certain small percentage of the cases of pulmonary tuberculosis such factors may control the situation and determine the outcome. However, in the vast majority of cases the outcome is not de-

termined by these more or less fixed factors, but by the more important variable or changeable factors which change or vary according to the psychology of the patient. It is these changeable factors which may and should come under the immediate control of the physician. And this is where we as physicians, entrusted with the responsibility of guiding patients with pulmonary tuberculosis back to health, find our opportunity, for the most part, to discharge that responsibility.

While the diagnosis of early tuberculosis is not an easy matter, yet, the diagnosis having once been made, the most serious task and responsibility of the physician remains. In every branch of medicine the physician must assume full responsibility for his patient. In tuberculosis this responsibility is not only great, but it is strenuous because of the nature of the disease and the nature of the cure with its long drawn out course. We should regard a patient with active pulmonary tuberculosis with the same seriousness with which we would regard a patient with acute appendicitis. The issue is the same in each case, that is, the outcome is uncertain and the life of the patient is at stake.

We cure tuberculosis by raising the resistance of the body against the inroads of the tubercle bacillus. The most important factor in raising this resistance is rest, and by rest we mean not only physical, but emotional and mental relaxation.

Generally speaking, the treatment of tuberculosis involves a mapping out of a mode of life with attention to details. The skill of the physician in determining the mode of life necessary for any particular case and his skill in influencing the patient to abide by that mode of life with an optimism and enthusiastic regularity measures his ability to influence favorably the prognosis of tuberculosis.

It is true that certain patients are so constituted temperamentally that, once the nature of the cure and the importance of its various phases are explained to them, they are able to follow it cheerfully and more or less rigidly. This, however, is not true of the average patient. To expect the average patient, who is accustomed to the duties and responsibilities of ordinary life, to suddenly give up his usual ways of doing and living and thinking and cure his tuberculosis after he has been simply advised that he needs a rest or that he must take life easy, is as impractical as it is to expect a ship that has been turned loose on the seas without a pilot to reach a given port.

Again, in pulmonary tuberculosis the nature of the disease is such that its poisons seem to affect the centers of nervous and mental control of those afflicted so that these centers are in a state of unstable equilibrium. We must realize, then, that we are not dealing with normal individuals, but with people who, for the most part, are not only physically, but mentally and nervously sick. In other words, if we as physicians are to do our duty in aiding these patients to recover their health, we must study them and understand them and supervise them so that we can control them mentally and emotionally. As we all know, the emotions have a very direct effect upon the functions of the body. Crile has said, "Emotions drive the organism with extreme intensity and may cause exhaustion or shock". He further adds

that at autopsy certain definite changes in tissues such as the brain, liver and other organs are found which are due entirely to the emotions. Likewise we are not able to control these patients physically until we first have them under control mentally and emotionally.

Many patients fail to make the proper effort to take the cure because they either have not been made to understand the seriousness of their condition or because they have not been made to understand what taking the cure means. Again, many patients who are extremely refractory when first told they have tuberculosis and what they must do to get well, often, in a relatively short period, prove to be excellent patients provided they are made to understand the situation as they should.

Many of the disturbing influences which interfere with the patient's progress once he is started on the cure, are the result of a state of mind. For example, patients who state that it is impossible for them to adjust themselves to the details of the cure because they are so nervous and who cannot eat or sleep and have an unproductive, racking cough, usually, after they have been reassured that these symptoms are not a serious indication, but are largely the result of a state of mind and that they have it within their own power to overcome them, are, for the most part, relieved of these conditions in a very short time. Those who deal with tuberculous patients not only continually witness such adjustments to the cure which come as the result of reassurance based upon a proper understanding of the facts, but they also see the marked improvement in the general condition of the patient, which results.

The physician, then, who deals with tuberculosis, must understand not only tuberculosis and its peculiarities, but he must also understand human nature and its various peculiarities, because it is on his ability not only to properly understand and control his patient, but to buoy him up and inspire him to cheerfully continue for perhaps months or even years what would otherwise seem a monotonous and hopeless task that a favorable prognosis often rests.

Our control of the patient's mental and emotional state is secured by our attitude toward the patient, by our ability to impress him with our understanding of his disease and of his feelings and with our personal interest in his case, and finally by our ability to assist the patient in taking the cure in an environment wherein he is assisted in his physical, mental and emotional efforts to the utmost.

Our first step from a phychological consideration, which makes for a favorable prognosis, is to truthfully explain to the patient the extent of his disease as well as the nature and the purpose of the cure. The nature of the cure is such that unless patients understand their condition thoroughly and what they must do to recover their health, they cannot follow it as they should. It is the uncertainties in life, whether they have to do with health or other serious matters, that cause worry, restlessness, and emotional disturbance, and a simple, but frank explanation of the facts goes a long way toward establishing that bond of confidence which should exist between patient and physician. At the same time, there are very few patients who cannot face the truth if it is put up to them optimistically. The patient and his rela-

tives must be made to understand that the patient is the one who must take the cure and that the physician's duty is to aid him by advice and intelligent guidance.

In administering this advice and guidance, the physician must so place the patient that he will be aided by his environment. We are all more or less the products of environment and this is particularly true of patients with tuberculosis because of the nature of the life they must lead and because of the unstable condition of their centers of control. Consequently, tuberculous patients are better able to carry out the necessary details which make for a favorable prognosis when they are so placed that they have the moral support and mutual sympathy of those around them and when they are under the continuous care and supervision of those who understand and appreciate their mental and nervous disturbances. Experience has proven that patients who take the cure surrounded by those who do not appreciate the nature of tuberculosis and the particular effect it has upon the patient and the importance of a detailed, enthusiastic mental cooperation on the part of the patient, in general have a less favorable prognosis. Their efforts at taking the cure are very often haphazard and too often they give up even those efforts before their condition warrants anything like a favorable prognosis. That is, they do not stay on the cure long enough and, while some of them under these circumstances may be able to get by for months or a few years, they eventually break again because they have not given themselves time enough to get a permanent arrestment.

In tuberculosis there is no factor more important in the prognosis than time. Many patients who would otherwise recover lose their lives because they do not stick to the cure long enough. With few exceptions, patients who give up the cure too soon do so because we have not instilled into them the right prospectus of tuberculosis and the essentials for its cure. That is, we have failed to influence their train of mind so as to hold them on the cure.

The length of time that it is necessary for any patient to stay on the cure is an individual matter. It must be sufficient, however, to give that patient an opportunity to demonstrate that he can or that he cannot overcome his disease. The physician must make the decision as to how long that time should be. This decision should be made not upon the feelings and appearance of the patient, but upon a thorough understanding of the patient in general and particularly upon a proper knowledge of the underlying pathology.

In conclusion, I think we should remember that while we regard tuberculosis as one of the most curable of chronic diseases, that the prognosis in the average case of active pulmonary tuberculosis is, at any given time, uncertain. It is uncertain because it is dependent on so many different factors. The more important of these factors which determine the prognosis vary with the psychology of the individual patient. This psychology depends, for the most part, upon the physician. Consequently, our ability to properly advise, to intelligently guide and to efficiently manage our patient is the outstanding influence in bringing about a favorable outcome in pulmonary tuberculosis.

Digestive Diseases and the Teeth

By William Lintz, M. D., *Brooklyn, N. Y.*

IN A personal communication, Dr. C. H. Mayo makes a statement that "75% of human ailments come from what goes into the mouth including food and drink, and the diseases of the mouth which cause local and general disease, and focal infections which may remain a cause of disease over a long period of time." From this statement it is at once apparent how important is a study of the teeth in disease in general and in digestive diseases in particular.

Cases For Investigation

Out of 361 consecutive office patients (See Table III) suffering with the various ailments for which they consult an internist, 150 were found to suffer from digestive diseases (See Table I). These constitute the basis of our study. The remaining 211 patients as well as 100 normal people (See Table II) are used as controls. Every tooth of these 461 people was carefully examined and the condition of the remaining was noted. Needless to say that everything possible was done to establish the correct diagnosis. This included not only a careful history, physical examination, laboratory investigation and X-ray examination, but operative findings where operation was resorted to for one reason or another. Missing teeth were regarded mainly as infected teeth for this was principally responsible for their loss, either spontaneously or by extraction. As a rule it was found where a patient had many teeth missing that the remaining ones were in bad shape and conversely where few were missing the remaining ones were in much better condition. This is explained by the fact that as a rule people hate to part with all their teeth and dislike wholesale extraction even when indicated; also by the fact that the malocclusion resulting from the loss of a great many teeth leads to deterioration and infection of the remaining ones.

Very few patients in this series were ultimately labeled with only a single diagnosis. The majority had more than one. The missing teeth are classified under each one of the diseases. This does not in any way invalidate our statistics, as this was accounted in the ultimate conclusion. The digestive disease was the predominating one in every one of the cases of this series.

When in a certain disease, the great majority of patients have a high percentage of missing teeth and the remaining ones in poor condition, inference may be drawn that there is an etiological relationship between the infected teeth and the disease. To point out this etiological relationship as well as its limitations as gathered from

TABLE I—DIGESTIVE DISEASES AND THE TEETH

DIAGNOSIS	Number of cases	Upper Jaw: Central Incisor	Upper Jaw: Lateral Incisor	Upper Jaw: Canine	Upper Jaw: Bicuspid	Upper Jaw: Molar	Lower Jaw: Central Incisor	Lower Jaw: Lateral Incisor	Lower Jaw: Canine	Lower Jaw: Bicuspid	Lower Jaw: Molar	Total—Both Jaws	Average per patient	Percentage
Cirrhosis of Liver	6	10	10	9	18	28	6	6	6	12	25	130	21	65 %
Cancer	7	10	10	10	16	31	6	7	7	15	32	144	20	62 %
Peptic Ulcer	26	15	16	17	48	74	15	16	14	42	80	337	13	40½%
Gall-Bladder Disease	120	86	93	55	217	364	50	46	49	138	237	1335	12	37½%
Constipation	15	8	8	8	24	45	6	6	6	26	44	181	12	37½%
Appendicitis	49	26	25	25	76	126	16	12	12	48	120	486	9	28 %

Total Number of Missing Teeth in Sequence

Upper Jaw		Lower Jaw		Both Jaws	
Molar	668	Molar	538	Molar	1206
Bicuspid	399	Bicuspid	281	Bicuspid	680
Lateral Incisor	162	Central Incisor	99	Lateral Incisor	255
Central Incisor	155	Canine	94	Central Incisor	254
Canine	124	Lateral Incisor	93	Canine	218
Totals	1508		1105		2613

The average loss was 11.7 teeth per patient.
The average rate of loss was 36.5% per patient.
There were 36.4% more upper teeth lost than lower.

TABLE II—MISSING TEETH IN NORMAL PERSONS

	AGE	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50	50-55	55-60	60-65	65-70	
	Number of cases	15	9	15	17	12	10	10	5	3	1	2	1	100
Upper Jaw	Central Incisor	2	2	3	..	5	10	5	2	..	2	..	2	33
	Lateral Incisor	2	2	2	2	4	10	7	2	..	2	..	2	35
	Canine	..	.	..	..	7	8	6	3	..	2	2	2	30
	Bicuspid	1	.	2	2	11	19	13	6	3	4	1	4	66
	Molar	1	2	12	6	25	38	24	15	7	6	2	6	144
Lower Jaw	Central Incisor	..	.	..	..	..	8	6	2	..	..	..	2	18
	Lateral Incisor	..	.	..	..	..	7	7	3	..	..	..	2	19
	Canine	..	.	..	..	1	8	6	1	..	..	1	2	19
	Bicuspid	3	.	..	..	7	16	15	3	..	..	1	4	49
	Molar	..	2	14	7	31	28	28	9	8	3	3	6	139
	Total Missing	9	8	33	17	91	152	117	46	18	19	10	32	552
	Average per person	.6	.9	2.2	1.0	7.6	15.2	11.7	9.2	6.0	19	5	32	5.5

	No. of cases	No. Missing Teeth	Per Cent Missing Teeth
Males	48	242	15.8%
Females	52	310	18.7%
Both sexes	100	552	17.2%

Total Number of Missing Teeth in Sequence

Upper Jaw		Lower Jaw		Both Jaws	
Molar	144	Molar	139	Molar	283
Bicuspid	66	Bicuspid	49	Bicuspid	115
Lateral Incisor	35	Lateral Incisor	19	Lateral Incisor	54
Central Incisor	33	Canine	19	Central Incisor	51
Canine	30	Central Incisor	18	Canine	49
Total	308	Total	244	Total	552

The average loss was 5.5 teeth per patient.
The average rate of loss was 17.2% per patient.
There were 26.2% more upper teeth lost than lower.

actual detailed experience obtained from the patient, but which is greatly underestimated and under utilized, or conversely abused by the profession in the treatment of digestive diseases, this paper is written.

Cirrhosis of Liver

There were six patients in this group; each one had lost on the average 21 or 65% of the teeth. This is rather high. At first glance it seems to be contrary to medical experience to associate cirrhosis of the liver with focal infection. But if one bears in mind the universally admitted relationship between dental infection and the gall-bladder and biliary duct pathology and that these in turn are frequently a factor in cirrhosis of the liver[1], this apparent incongruity becomes understandable. Another factor enters here which makes these figures so high. I believe that this is one of the diseases where needless extractions are performed on account of the difficulty of establishing the diagnosis[2] and the unsatisfactory therapeutic results. When either one or both of these factors exist, I find that not a few doctors will resort to needless teeth extraction, with the hope of influencing favorably certain existing symptoms. It is therefore advisable to bear in mind the diagnosis of hepatic cirrhosis in cases of dubious pathological indications for dental extraction, which leads to negative results for the relief of symptoms of indigestion. As this is a disease of later life the age factor must also be considered (See Table III). I have no experience with the eradication of focal dental infection in this disease but in the future, I believe in view of the high percentage of missing teeth it would be worth our while to pay more attention to the teeth in this disease.

Cancer of Stomach

There were seven patients in this group, each patient had lost on the average 62½ percent of his teeth. I do not believe that this implies an etiological relationship. The reason for the wholesale extraction is chiefly in mistaken diagnosis particularly at the beginning of the disease. The teeth are removed because these patients are diagnosed frequently as ulcer of the stomach, chronic cholecystitis, appendicitis, etc.; in other words, those diseases in which we have a right to expect good results from the eradication of focal infection (see below). It behooves us therefore in the above mentioned diseases when wholesale dental extraction leads to unfavorable results to retrace our steps that have led to such a diagnosis and to double our vigilance for gastric carcinoma. Age is also a factor in this disease. (See Table III).

Peptic Ulcer

Over 40 percent of the teeth were missing on the average in each of the twenty-six cases comprising this group. The remaining teeth as a rule were in bad shape. While very few clinicians of experience doubt the close relationship of infected teeth to peptic ulcer, the great majority of surgeons are exceedingly skeptical about this point and pay very little attention to it. Yet this factor is of vital importance for obtaining results in this disease both along medical and surgical lines. Remove the focal infection and the ulcer shows

The average ratio of loss was 7% for the lower jaw. There were 26.2% more upper teeth lost than lower.

TABLE III—MISSING TEETH IN DISEASE

AGE	Number of cases	Upper Jaw					Lower Jaw						
		Central Incisor	Lateral Incisor	Canine	Bicuspid	Molar	Central Incisor	Lateral Incisor	Canine	Bicuspid	Molar	Total	Average
5-10 years	11	..	..	..	..	...	..	1	..	1	5	7	—1
10-15 years	9	2	..	..	..	4	..	..	..	2	2	10	1
15-20 years	20	3	2	..	4	7	..	..	..	2	13	31	1
20-25 years	32	6	7	4	18	20	2	2	2	16	35	112	3
25-30 years	31	..	3	2	11	29	2	1	..	3	29	80	2
30-35 years	51	11	16	17	41	91	2	2	5	36	110	330	6
35-40 years	42	13	12	13	53	92	4	4	6	35	120	352	8
40-45 years	34	27	27	26	27	98	7	8	9	35	97	401	11
45-50 years	32	25	27	26	58	96	16	16	15	48	108	435	13
50-55 years	30	39	35	34	80	130	28	22	21	59	100	548	18
55-60 years	22	21	23	22	52	83	18	11	8	38	84	360	16
60-65 years	21	38	38	35	72	109	34	32	34	75	113	580	27
65-70 years	8	12	14	12	21	39	13	15	11	25	45	207	25
70-75 years	4	8	8	7	15	22	8	8	8	16	23	123	30
75-80 years	1	2	2	2	4	6	2	2	2	4	6	32	32
80-85 years	1	2	2	2	4	6	2	2	2	4	6	32	32
Total Cases	349												

Total Number of Missing Teeth in Sequence

Upper Jaw		Lower Jaw		Both Jaws	
Molar	832	Molar	996	Molar	1,678
Bicupid	500	Bicupid	399	Bicuspid	899
Lateral Incisor	215	Lateral Incisor	138	Central Incisor	347
Central Incisor	209	Central Incisor	126	Lateral Incisor	341
Canine	202	Canine	123	Canine	325
Totals	1,958	Totals	1,682	Totals	3,640

The average loss of teeth was 10.4 per patient.
The average rate of loss was 32% per patient.
The rate of loss was 16.4% more in the upper jaw than in the lower.

great tendency to heal. This is true not only in cases of recent origin, but in old chronic cases of long standing as well. Any treatment no matter how thorough is less than half completed unless it includes the eradication of any present focal dental infection. Very often all symptoms completely and permanently disappear when this is performed without any other treatment. This, of course, does not necessarily mean that the teeth are always responsible. The infection may be in the tonsils, sinuses, or any other part of the body. This holds good not only in this disease but in any other disease. But in view of our dental statistics of members of this group which we interpret as exhibiting a high degree of infection both in the past and in the present, backed by therapeutic experience and the results obtained in a large number of cases, I believe that the infected teeth in particular play the most important rôle in this relationship.

Every diagnosis of peptic ulcer must be accompanied by a roentgenogram of the teeth, and that irrespective of their apparent condition. For only too often one finds an abscessed tooth or granuloma in what appears to be a perfect set of teeth. This is usually more than sufficient to cause and account for the ulcer. I find that delay in therapeutic results and recurrences are due to infection which has not been completely eradicated. Autogenous vaccine administration in sufficient dosage to produce moderate local and general reaction, irrespective of the number of bacteria injected, I find an important adjuvant in this treatment.

The following typical case beautifully illustrates some of the enumerated points:

E. K., male, 41 years old, lost 35 lbs. in weight, had been suffering periodically for two years with indigestion, occasional vomiting spells and very severe epigastric pain which sometimes penetrated to the back, and very often awakened him from sleep. On physical examination with the exception of epigastric tenderness he was essentially negative. The routine blood and the Wasserman were negative. The blood sugar was 0.18%. A marked glycosuria, acetone, diacetic acid and B-oxybutyric acid were found. The gastric chemistry, feces examination, fluoroscopy and X-ray of the entire gastrointestinal tract were typical of a duodenal ulcer. Cholecystography was negative. Multiple abscessed teeth were discovered on roentgenologic examination. Upon the eradication of all dental infection before any other treatment was instituted all symptoms promptly vanished. Under the proper dietetic regime, medication, insulin and the proper administration of autogenous vaccines permanent relief of all symptoms has been established.

Comment: A diabetic, suffering from a large duodenal ulcer of two years standing promptly experienced relief of all symptoms upon the extraction of infected teeth. This resulted in a permanent cure when the usual treatment for this condition was instituted. Autogenous vaccine, prepared from the dental infection was employed.

Gall-Bladder Disease

Under this heading are grouped 120 patients who suffered mainly from cholecystitis, a few from the acute form, and 12 cases of cholelithiasis. Although practically every one of these cases has been studied most thoroughly including a roentgenologic dye investigation, the usual difficulties en-

The average loss of teeth was 10.4 per patient.
The average rate of loss was 32% per patient.
The rate of loss was 16.4% more in the upper jaw than in the lower.

countered in differentiating gall-bladder pathology with stones from that without stones has also here been encountered. However, from the point of view of dental infection it does not matter, since the former is very often the offspring of the latter and both have as a rule an identical etiology. In a few cases the diagnosis was confirmed by surgery.

In gall-bladder disease infection plays an important rôle. Out of 120 patients, each one had lost on the average 37½ percent of his teeth as compared with over 42 percent in peptic ulcer. In general, whatever has been said under peptic ulcer holds good here. I have seen again and again all symptoms ameliorate or even disappear immediately and quite often permanently upon the complete eradication of focal infection. Under this heading dental infection plays an important rôle. Failure to eradicate focal infection or to remove it completely is frequently responsible for unsuccessful results in the treatment of gall-bladder disease both medically and surgically. I know of no better way of obviating surgery in gall-bladder pathology than by the removal of focal infection. In this disease as well as in peptic ulcer I believe that better and more permanent results are obtained if along with the usual treatment the administration of autogenous vaccines made from the infected focal infection is performed. Twelve injections repeated after an interval of three months usually gives sufficient immunization. As this is, as a rule, a chronic disease, vaccine therapy is particularly suitable. The treatment of gall-bladder disease by this thorough, complete method, obtains quite often results which exceed our fondest expectation.

The following case from actual practice amply illustrates the considerations just made:

G. S., female, 51 years of age had been suffering for over 10 years with periodic attacks of pain over the right side and back and right hypochondrium. Indigestion was a marked symptom; occasional nausea, vomiting and headaches were present. She gave a past history of having had a partial ovarian resection for cyst, operation for retroversion of uterus and for chronic appendicitis with no relief of symptoms. On physical examination she was 35 lbs. overweight, her blood pressure was 170/120, her basal metabolic rate was —31%, and she exhibited all the objective signs of gall-bladder disease. The gastric analysis, urine, feces and blood, including the Wasserman test were negative. X-Ray examination of the gastro-intestinal tract and kidneys was negative. Cholecystography revealed a chronic cholecystitis. Her teeth showed considerable dentistry. She told me that they were "all right" and that they were continuously being looked after by a dentist of repute in whom she had great confidence. Her weight was reduced to practically normal under the proper endocrine therapy and diet. She was placed under the usual medical gall-bladder treatment with indifferent results. A dental check-up was insisted on which showed on roentgenologic examination retained dead roots, dead teeth and several abscesses. Meanwhile one of the teeth became acutely inflamed and had to be extracted. Immediately there was a disappearance of all symptoms and when all the infection was eradicated and autogenous vaccine immunization instituted this stubborn case was promptly cured by medical treatment.

Comment: 1. Patients with focal infection are the subjects of frequent operations which in the main are unsuccessful.

2. Not infrequently the doctor is mislead by poor dental work. Many dentists do not understand and even

ridicule the importance of focal dental infection.

3. When poor results are obtained in the treatment of the above-mentioned digestive diseases re-check your diagnosis and double your vigilance and search for focal infection.

4. The eradication of focal infection and subsequent immunization will prevent useless surgery and turn failure into success.

Constipation

15 patients in this group, each one had lost on the average 37½ percent of their teeth. This emphasizes the importance of bad teeth in digestion and the production of gastro-intestinal pathology responsible for constipation. The harmful effects of bad teeth in this condition is twofold, namely, mechanical, resulting in faulty mastication and the consequences which follow this, and metastatic dissemination and toxic absorption from the infected dental areas giving rise to the various pathology in the digestive tract which in turn leads to constipation. At times one sees striking results from this disease from the eradication of all focal infection.

Appendicitis

49 patients constituting this group who had over 28 percent of their teeth missing were practically all suffering from the chronic type of this disease. More upper teeth were lost than lower and arranged numerically they have the same striking sequence in both jaws, namely, molars, bicuspids, central incisors, with equal losses of the lateral incisors and the canines. This order holds good in all diseases and even in normal people. From clinical experience I believe there is a definite etiological relationship between focal infection and chronic appendicitis. No treatment is complete whether medical or surgical without thorough eradication of dental infection. The reason why the end results of both medical and surgical treatment are so unsatisfactory[3 4] is because foci of infection are not completely eradicated whether they be in the teeth or elsewhere. (See case cited under gall-bladder disease).

Conclusion

1. Office patients suffering from digestive diseases have lost on the average 36.5 percent of their teeth, compared with normal people (see Table II) who have lost 17 percent and with those from the various medical ailments who have lost 32 percent of their teeth (see Table III).

2. There is a definite etiological relationship to a much greater extent than heretofore supposed between focal dental infection and digestive diseases. The removal of focal infection is therefore indicated in its treatment whether that be medical or surgical.

3. So gratifying is the outcome that where unsatisfactory results are obtained, double your search for incomplete eradication of focal infection or be on the lookout for mistaken diagnosis.

4. The eradication of focal dental infection will frequently obviate surgery.

5. In health or disease more teeth are lost in the upper than in the lower jaw. In digestive diseases this amounts

to 36.4 percent. All teeth are lost in a definite sequence, namely, molars, bicuspids, central incisors, lateral incisors and canines.

6. The administration of autogenous vaccines made from the infected focal areas is a valuable adjuvant in the treatment of digestive diseases.

7. Peptic ulcer has a great tendency to spontaneous healing upon the removal of focal infection.

8. The unsatisfactory results from the medical and surgical treatment of chronic appendicitis can be frequently attributed to failure of recognizing and eliminating focal infection.

9. The medical treatment of gallbladder disease is very satisfactory providing focal infection is completely removed and autogenous vaccine administration is practiced.

10. The physician is frequently mislead by the dentist who is ignorant of and even ridicules the importance of focal infection. Personally examine every dental roentgenogram. The cooperation of the dentist is absolutely essential for success in this work.

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Tropical Sprue*

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In THE past five years we have had 36 cases of tropical sprue here, usually missionaries returned from the Orient. Before that time there were records of 15 cases among our patients. A great deal has been learned from a study of these cases, many papers appearing during this time on various aspects of the disease. We also have published different findings as they occurred in our cases.

We began our study of this condition with no preconceived ideas of any phase of the disease, as a matter of fact in gross ignorance of the entire subject except the name. One attempts generally to keep free of such handicaps to careful study. But in time we absorb and accept ideas that soon may become as pernicious as any preconceived idea.

There are many phases in the study of any disease. One soon becomes more engrossed in one than in another, with at least apparent neglect of other phases equally important. Our sin in the studies of tropical sprue has probably been the common one in this country in medicine of today: over emphasis of the laboratory side. Another equally common mistake has been too many publications in an already crowded field. However, we believe that our studies have called attention to several (four) points in sprue, and they have resulted either in confirmation of other work or in establishing new points.

There is still no definite knowledge of the cause of this disease. Osler[1] very wisely gave several of the current theories. They may still be considered current. Ashford[2] at first believed his monilia X, (Monilia psilosis) was the cause. Recently this author[3], agreeing with Scott's[4] work on the low blood calcium occurring in some cases, has been inclined to believe some kind of deficiency also is necessary. The British as a whole, like many other workers on this disease, have not taken too kindly to Ashford's monilia as a cause of sprue (Low[5, 6]). We were at first strongly tempted to this view[7]. In our further studies this organism was found in a smaller percentage of cases. It has, however, been found in culture of the stools in 23 of the 36 cases[8] and in 9 others an organism slightly atypical was found. In 16 cases, the most severe and anaemic of the 36, there were positive cultures repeatedly in every case, although in two the organism was not quite typical in that maltose was not fermented. When we began our first culture work on sprue

*This paper is written as an introduction and as a summarizing paper to a series of papers from the Clifton Springs Sanitarium and Clinic appearing in various journals in the past five years.

stools we had had no experience in this type of bacteriological study. In our first case we succeeded in growing the Monilia psilosis. We have thus in this series confirmed Ashford's work that this organism may be grown from a large per cent of sprue cases.

Is this organism only a secondary invader as some (Low) believe? Recent experimental[9] [10] work has not confirmed Ashford's[11] and Smith's[12] earlier studies. A few attempts here with feeding the organism to rabbits caused an infestation but no disease. Intravenous injections of sufficiently large amounts of the culture caused early death of the animal with emboli in spleen and liver, causing no sprue. We admit the possibility of the wrong laboratory animal being used, but no others were available. We doubt whether monilia is the true cause of sprue but we feel more certain of our diagnosis if monilia can be obtained by culture from the stools. We have not confirmed the large percentage of positive cultures in pernicious anaemia[13] and psoriasis (unpublished work) obtained by Wood[14], and Fleisher and Wackowski[15].

The pathology is certainly not specific. We believe the small liver and thin intestinal wall are only evidence of the extreme loss of weight seen in the cases that die of this disease. The translucent edematous serous surfaces[16] [17] also are probably results of starvation. The enlarged mesenteric nodes may possibly be due to reaction to monilia. No monilia was found in them in our case, nor in the intestinal wall. Iron pigment, like that found in pernicious anemia, occurred in the liver in our case, but on examination the bone marrow was hypoplastic. Perhaps Lambert[18] will have found something more definite when he publishes his necropsy cases, certainly Mackie and Fairley[19] in a wider experience than ours, have not.

The symptoms and physical findings are classic. The very definite tetany or marked Chvostek and Trousseau signs seen in some cases are pathognomonic under certain conditions.

The severe anemia has been noted repeatedly. In our experience the blood picture of the cases with severe anemia differs from that in pernicious anemia in only two points, the Arneth count[20] [21] and the few nucleated red cells present. We have found in sprue that the Arneth count is the same as in the normal. In our 16 severely anemic cases only two, like the cases with pernicious anemia, showed a shift to the right in the Arneth count. Both of these had free hydrochloric acid in the gastric fractional tests. In a third case one of two smears counted showed such a shift. This patient had a negative alkaline tide (probable evidence of achlorhydria, Hubbard[22]) and had also a low blood calcium and tetany reactions. Serra[23] found a low Arneth count in 10 cases of sprue, presumably like that in a pernicious anemia, Fleming[24] found the shift to the right in 2 cases as did Krjnkoff in a study of some cases.

The icterus index in the tested cases (20) was slightly higher in the more severely anemic patients than in the whole group. Serra found a low index in 6 cases, and Newham[25] a positive Van den Bergh in 7 cases like in pernicious anemia. Fairley and his co-workers[26] found the blood bile pigments low

rather than high as in cases of pernicious anemia. In our work here, too, the icterus index in a group of 10 cases of pernicious anemia has shown a higher figure (16.9) than in our sprue cases with severe anemia (10.6).

What then is the difference in the blood disease of sprue and pernicious anemia? We confirm Fairley and his co-workers that there is, according to blood bile pigments, less evidence of hemolysis in sprue than in pernicious anemia. The bone marrow in sprue does not show the marked hyperplasia seen in pernicious anemia, shown by autopsy[17, 19] and also by the less frequent occurrence of nucleated red cells[20, 26, 27]. As many lobed nuclei are evidence of older neutrophiles this points to slow formation or, (and), slow destruction of this type of cell in pernicious anemia. But in sprue the Arneth shift is not to the right; the neutrophiles appear like the normal. Is there a toxin acting especially on young granulated white cells in pernicious anemia? The selective action must be very close if we consider these like the erythrocytes arising from the same primordial bone marrow cell.

The low blood calcium sometimes found in sprue cases is definite even though Ashford[28] and Hernandez found this occurs also in other tropical conditions or in many chronic gastro-intestinal states in tropical countries. Certainly our low blood calcium figures have been from our sprue cases, of which almost half (11 of 30 cases) showed low blood calciums, and in four of these very low calcium figures (8). In this we confirm Scott and others who found cases with low calciums. One wonders how closely this is related to calcium loss from diarrhea. Figures on the number of stools in our cases are not available, and impressions from memory in medicine are not to be relied upon. Studies of the fats in stools were made in a few of our cases, but the figures obtained varied widely. Certainly though, Linder and Harris'[29] work shows some relation to fat metabolism. Some quickly acting costive agent might be of value in the case in extremis. We believe parathyroid extract (Collip) helps these cases, it undoubtedly raises the blood calcium[30]. It seems strange that these cases may not respond to intravenous calcium therapy as occurred in Bovaird's case[31]. No response to this treatment was had in one of our cases[30] but most unfortunately for us the patient was no longer under our care. Recently Holmes and Starr[32] have described some sprue-like cases with low calcium figures, which were improved with parathormone.

Thayseen and Norgaard[33] have found a low blood sugar curve after glucose tolerance tests in cases of sprue. Fasting blood sugars were normal in all of our cases tested (21 cases). Gastric fractional studies show as a rule even in very severely anemic sprue patients a normal or occasionally a high acid content. Only 5 of our 16 cases with severe anemia had an achlorhydria (8) although two others had a negative alkaline tide while only two of the 20 cases with secondary anemia had an achlorhydria. Three out of 25 cases in Serra's series showed an achylia. Fairley's cases also rarely showed a lack of free hydrochloric acid. And yet Castle[34] described a sprue case with free hydrochloric acid which was not

efficient when mixed with beef in improving a pernicious anemia patient. His experiments on the effect of gastric contents of the normal individual in improving the pernicious anemia case are now well known.

We found the gastro-intestinal X-ray examination in many severe cases of sprue almost pathognomonic[8]; a dilated, elongated, atonic colon, often with few haustrations occurring so often among the cases in which the diagnosis of pernicious anemia seemed plausible. Such a colon is not seen in the latter disease. This also we have presented as a new point[8]. Holmes and Starr have recently described very similar findings in cases of "non-tropical sprue." Three of their four severely anemic cases had been in subtropic or tropics where sprue is found and sprue has been described as occurring in patients several years after leaving a tropical climate. Hunter[35], also, mentioned that a dilated colon was found in cases with disturbed calcium metabolism.

The diagnosis of sprue is often difficult but we have found the above points will usually differentiate it from the two conditions most to be confused, pernicious anemia and pancreatic disease. We have not been convinced that tropical sprue and pernicious anemia are the same disease, even when such students as Christian[36], Reed[37], and Wood have been arrayed in support of this view. However, Castle's recent work comes nearer than any other proving that the anemia of sprue and of pernicious anaemia are due to the same factors. We believe the anemia is a severe hypoplastic type but not aplastic as has been inferred by some[26].

We have found the high protein, low fat, low carbohydrate type of diet agrees with almost all cases. The liver diet used in pernicious anemia cases has been found just as efficient in the sprue patients with severe anemia[38, 39, 40] and a reticulocyte response similar to that in pernicious anemia has been reported. Ashford related that an increase in reticulocytes occurred following the use of his diet without liver, also after using monilia vaccine. We[41] found 9 per cent of reticulocytes in one case in which no liver had been used. Liver has no particular value in those milder cases with secondary anemia. It was often surprising to see how quickly a sore mouth would disappear without any other treatment than the above diet, or how soon a persistent anorexia gave way to a ravenous appetite. Three cases described by Hubbard and the author[42] show that the high protein diet did no further harm to damaged kidneys.

Even if we report 5 deaths in our series of 36 cases[8] we cannot subscribe to the gloomy views in prognosis expressed some years ago[37]. In our experience even the severe cases may be given a good prognosis if not for ultimate complete recovery, at least for recovery to useful life with no more handicap than to avoid certain excesses of diet. A handicap that is cheerfully observed by numerous diabetics.

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Note on the Systematic Effect of Hydrochloric Acid in Patients with Achlorhydria

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PHYSICIANS who feed hydrochloric acid to patients with achlorhydria sometimes seem to think that they are employing a form of replacement therapy as they do when they inject insulin into diabetics or when they feed thyroid to myxedematous subjects. Such similies are not correct. Hydrochloric acid secreted by the stomach is formed by the gastric glands from material in the blood stream. As a result of this withdrawal of acid ions the reaction of the body fluids tend to become more alkaline. Later the hydrochloric acid is neutralized in the intestinal canal. The ultimate source of the alkali for this purpose is usually the base in the body. Theoretically the amount of base liberated when hydrochloric acid is formed is approximately counterbalanced by the amount of base utilized in neutralizing that acid. The result of these processes is apparently a rhythm of changes in the alkalinity of the body the reverse of those occurring in the stomach. In achlorhydria this rhythm is absent for acid is not formed from the blood stream and therefore no excess base is produced to be utilized later in neutralizing it. If hydrochloric acid is fed to a patient suffering from this disease it must be neutralized by the body just as any acid or base ingested by a normal subject must be neutralized by his tissues. This process involves changes in the respiration and in the acidity of the urine which can be measured.

In the present note some data upon the acidity of the urine are given to illustrate the effect of feeding hydrochloric acid to patients with achlorhydria. Such figures show only part of the changes which take place, but they serve adequately to demonstrate the fact that rather marked changes in the metabolism can be brought about by giving rather small amounts of acid to such patients.

Case 1 shows a marked contrast between the reactions of two series of urines collected between 7 o'clock in the morning and one o'clock in the afternoon. The first test was done shortly after the admission of the patient, and the second one was carried out about two weeks later after acid treatment had been instituted. The same breakfasts were fed between 8 and 9 o'clock, and all other conditions were as nearly alike as possible, except that 1 dram (3.7 cc.) of dilute hydrochloric

*From the laboratories of the Clifton Springs Sanitarium and Clinic, Clifton Springs, New York.

acid was given with the meal during the second one. The urine was very much more strongly acid during the second test than it was during the preceding one.

Upon Case II a series of tests was run under carefully standardized conditions. Only the factors described below differed during the different periods. Test "A" was carried out when she was first seen. A diagnosis of achlorhydria was made at this time, and she was given a prescription calling for a dram (3.7 cc.) of dilute hydrochloric acid with each meal. Two months later the examination was repeated. The same breakfast was used, and hydrochloric acid was not given during the test period. The result "B" shows a marked increase in the acidity of the urine. In this instance, as in some others seen, the long administration of hydrochloric acid had apparently produced changes in metabolism which persisted when the usual dose was omitted. Test "C" was similar to test "B" except that the patient received her usual dose of 1 dram (3.7 cc.) of hydrochloric acid in a glass of orange juice with the test breakkfast. Under these conditions the urine showed a still greater degree of acidity than it did when the dose was omitted. Tests "D" and "E" are similar to test "C" except that the amounts of acid given were somewhat greater. For some days prior to test "D" 2 drams (6.4 cc.) of dilute hydrochloric acid were given with each meal, but on the morning of the experiment only 1 dram was furnished with the breakfast. In test "E" not only was the increased amount of acid given before the experiment, but the dose taken simultaneously with the breakfast was also 2 drams (6.4 cc.). It is evident that the degree of acidity of the urine roughly paralleled the amount of acid administered. Since the hydrochloric acid was given in orange juice, and since it is known that orange juice forms base in the body when it is used as a food, test "F" in which a glass of orange juice alone was added to the standard breakfast, was carried out. The figures show that the urine was less strongly acid upon this morning than on any other day when the patient was studied. Test "G" was performed as a final control upon the series. The regular breakfast was fed with neither acid nor orange juice added to it. The figures are almost identical with those obtained in test "B"—the first one carried through after the patient had been placed under hydrochloric acid therapy.

Results on Case III are shown to illustrate the effect of a breakfast containing alkaline forming foods fed to a patient who was free from achlorhydria. Exxperiment "IIIA" gives the average of the reactions found in six tests where the standard breakfast, consisting of a glass of milk, a glass of water, 2 slices of toast with butter, and an egg was fed; test "B" gives the result when the breakfast was made up of orange, grape-fruit, egg, bacon, and coffee. The urinary reaction was much less strongly acid when the fruit was eaten.

Case IV shows the contrast between a test carried out after 4 days upon a base-forming diet selected from standard food tables and one performed after an equal period upon unselect-

ed foods. The patient had had achlorhydria for a long time and had been receiving hydrochloric acid regularly for years. She took her usual dose with the standard breakfast in each of the two tests. It is evident that in experiment "A" which was preceded by alkaline forming foods, the urine was much less strongly acid than in test "B" which followed a period when the diet was more nearly of the usual type.

Conclusions

Urine strongly acid in reaction is excreted during the morning period by patients with achlorhydria who receive therapeutic doses of hydrochloric acid with the morning meal. Sometimes long-continued administration of hydrochloric acid is followed by the excretion of a strongly acid urine even when the acid is omitted on the day of the test. If alkaline-forming foods (citrus fruits) are given at breakfast time urine of a diminished degree of acidity is excreted during the morning. Administration of an alkaline-forming diet may decrease the acidity of urine excreted when hydrochloric acid is given. It seems worth while, when patients do not tolerate long-continued hydrochloric acid therapy well, or when they show any signs attributable to a disturbance of the acid-base balance of the body, to combine the therapy directed towards the gastric condition with any alkaline-forming diet to counterbalance the metabolic effect of the ingested acid.

Case	Test	Reaction of Morning Urine Specimens					
		7-8	8-9	9-10	10-11	11-12	12-1
		pH	pH	pH	pH	pH	pH
I	A	7.8	7.8	8.0	7.8	7.2	6.7
	B	4.9	5.2	5.1	5.3	5.0	5.1
II	A	5.5	5.5	5.7	5.4	5.6	5.1
	B	5.0	5.1	5.1	5.0	5.0	5.0
	C	5.0	5.1	5.0	4.9	5.0	4.8
	D	4.9	4.9	5.0	4.9	4.7	4.6
	E	4.9	4.8	4.8	4.8	4.7	4.7
	F	5.6	5.5	5.4	6.5	7.1	6.5
	G	5.6	5.1	5.0	5.0	5.0	5.1
III	A	6.0	5.9	6.2	6.5	6.5	6.7
	B	5.5	5.7	6.6	7.6	7.4	6.3
IV	A	6.1	5.6	5.8	6.1	5.5	5.2
	B	5.4	5.1	5.1	5.2	5.3	5.1

Method for Adjusting the Diet in Diabetes

By Curtis Bruen, M.D., *New York*

THE treatment of diabetes mellitus is a problem in quantitative chemistry.

In functioning the organism exacts a certain output of energy from the metabolism of foodstuffs. This caloric requirement is equal to the basal metabolism, plus a percentage increment for the specific dynamic action of food, and a percentage increment for activity over and above basal. In order to meet this requirement the several foodstuffs must be metabolized in such amounts as correspond to the dietary equation

$$C=4.1\ CH+4.1\ P+9.3\ F \quad (1)$$

in which C represents calories per day, CH, P and F, grams of carbohydrate, protein, and fat respectively, and the coefficients, their respective standard values of calories per gram.

The growth and upkeep of tissue call for a supply of its constituents Ample allowance of protein, more especially during periods of increase, may safeguard against deficiency of whatever amino-acid is requisite. But for maintenance protein intake need only equal the wear and tear quota. The undue stimulation certain of its metabolites exert on the total metabolism makes it economical to keep protein consumption down to the minimum for nitrogenous equilibrium.

Diabetes is primarily a curtailment of the capacity to store and utilize the glucose equivalent yielded in the digestion of carbohydrate and the metabolism of protein and fat. An excessive increase and sluggish or arrested recession of the blood sugar follows its supplementation. It assumes an over-high post-absorptive base level. As often as its fluctuations overflow the renal threshold it spills over into the urine until the threshold concentration is regained.

The maximum glucose equivalent which can enter the blood stream during the absorptive period compatibly with normal disposition might be determined by the use of appropriately graded test-meals and standards. When post-absorptive hyperglycemia prevails, a given glucose yield can only be placed within, at, or beyond the prevailing capacity to metabolize it according as the post-absorptive hyperglycemia is depleted, sustained, or augmented. Such an influx of glucose as is consistent with normally sugar-free urine does not give rise to such fluctuations of the blood sugar as infringe upon the renal threshold.

Glucose equivalent tolerance, whether taken as the maximum which can be normally handled, or as the maximum which can be burned, is then practically an indeterminate quantity.

Still it is in turn skirted, encroached upon, and passed as sugar delays in the blood, accumulates there, and discharges into the urine. By trial it can be made out where a given intake at any one time stands in relation to these criteria. But the limits of normal disposition and of combustion cannot themselves be gauged. They need only be avoided.

In their metabolism protein, carbohydrate, and fat are mutually interdependent. With certain mixtures of the several foodstuffs metabolizing such a molecular ratio is maintained between typically fatty acid and glucose metabolites as just suffices to forestall the accumulation and excretion of acetone bodies. At the threshold of ketosis ketogenic and antiketogenic metabolites oppose each other in equimolecular proportions.[1] Since the average molecular weight of the more common fatty acids is 270 and the molecular weight of glucose is 180, the molecular ratio of 1 : 1 is equivalent to the weight ratio of 1.5 : 1, when ketogenic and antiketogenic precursors are calculated as fatty acid and glucose. Since, in the absorption of carbohydrate, the splitting of fat, and the intermediary metabolism of protein, these several foodstuffs yield fatty acid and glucose equivalents in the proportions.

$$\frac{\text{Fatty acid}}{\text{Glucose}} = \frac{0.46\ P + 0.9\ F}{CH + 0.58\ P + 0.13}$$

they must be metabolized in such amounts as satisfy the equation.

$$F = 2\ CH + 0.546\ P \qquad (2)$$

in order to maintain ketogenic-antiketogenic balance[2].

With a protein quota assigned, both the caloric requirement and ketogenic-antiketogenic balance are met by the metabolizing mixture which corresponds to equations (1) and (2) satisfied simultaneously.

Such a metabolizing mixture provides sufficient calories and avoids ketosis with a minimum glucose equivalent. It is the theoretical limit of insulin withholding. Hypodermic insulin fortifies and reinforces the capacity for glucose storage and utilization. When the glucose equivalent of this metabolizing mixture exceeds the existing capacity for its metabolism it is necessary to establish a new capacity pharmacologically.

Once the formulation is worked out and the calculations are set down it is well to look into how the application squares with what actually goes on.

The protein allowance need not be adjusted to the total nitrogen excretion but may be set at an empirical minimum of grams per unit of body weight for positive balance.

The normal basal metabolism (Chart 1) is subject to known variation. Conditions associable with diabetes alter the basal. The specific dynamic action of a given meal cannot be calculated because it depends in part on the nutritional conditions it encounters in the organism. The caloric demands of activity over and above basal can only be arbitrarily assumed. As a result only a preliminary approximation can be made of the total caloric requirement. This initial estimate can however be readily enough checked or corrected over a period of time in accordance with the declining, constant, or increasing body weight.

With the protein allowance assigned, and the caloric requirement estimated,

a diet may be calculated for ketogenic-antiketogenic balance, and adjusted to the capacity to utilize glucose and the ability to avert ketosis (Chart 2). The threshold test-diet may be liberalized to that extent, which, with the urine sugar-free, gives the best values of blood sugar and blood lipoids. If glucose metabolism is inadequate to even the equivalent of the threshold diet, its carbohydrate may be still further restricted under control of urinary tests for the acetone bodies by using values beyond the threshold. Ketosis alone makes insulin imperative. Or a diet inside the threshold may be used initially and modified in whichever direction is indicated. Once a suitable maintenance diet is determined its fat may be deleted so that deposit fat replaces it in the metabolizing mixture in order to reduce the body weight.

The standard caloric values of ingested foodstuffs are conventional averages which work out reliably taking into account their incomplete availability and absorption.

Actual menus are at best planned from approximate tables of food content.

Some portion of the food absorbed is not burned. It is used as raw material or laid down. The non-caloric food of growth and glandular elabora-

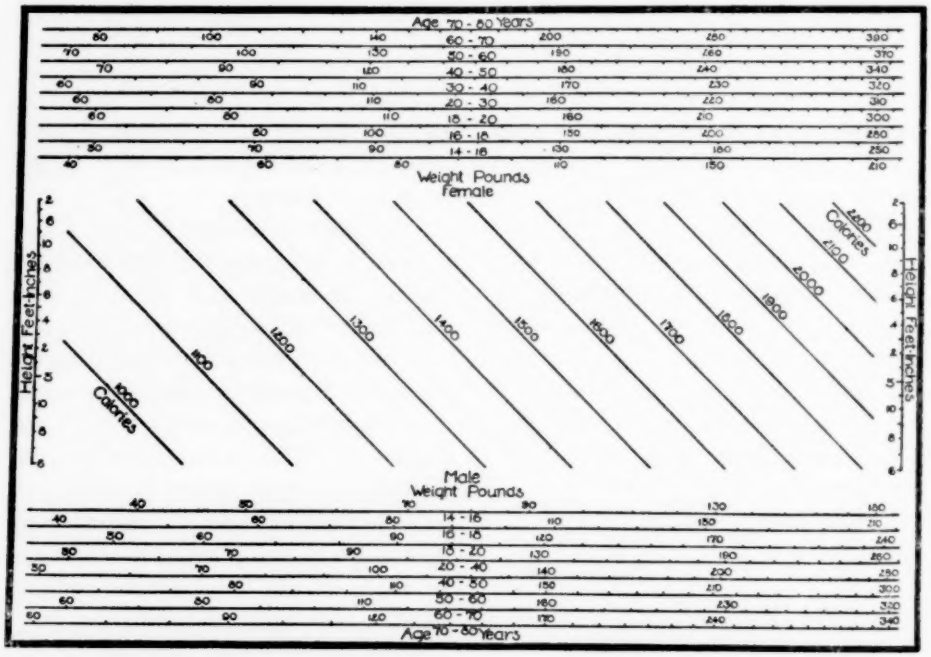

Chart 1.—Basal metabolism per day (Du Bois)[3]. Go to the upper tier of weight scales for females, to the lower for males; identify the scale for the required age group; spot the weight in pounds; carry a line perpendicularly into the field of the chart; spot the height in feet and inches on the nearest scale; carry a line horizontally to its intersection with the vertical line previously traced; approximate the number of calories by interpolating between the adjacent graphs.

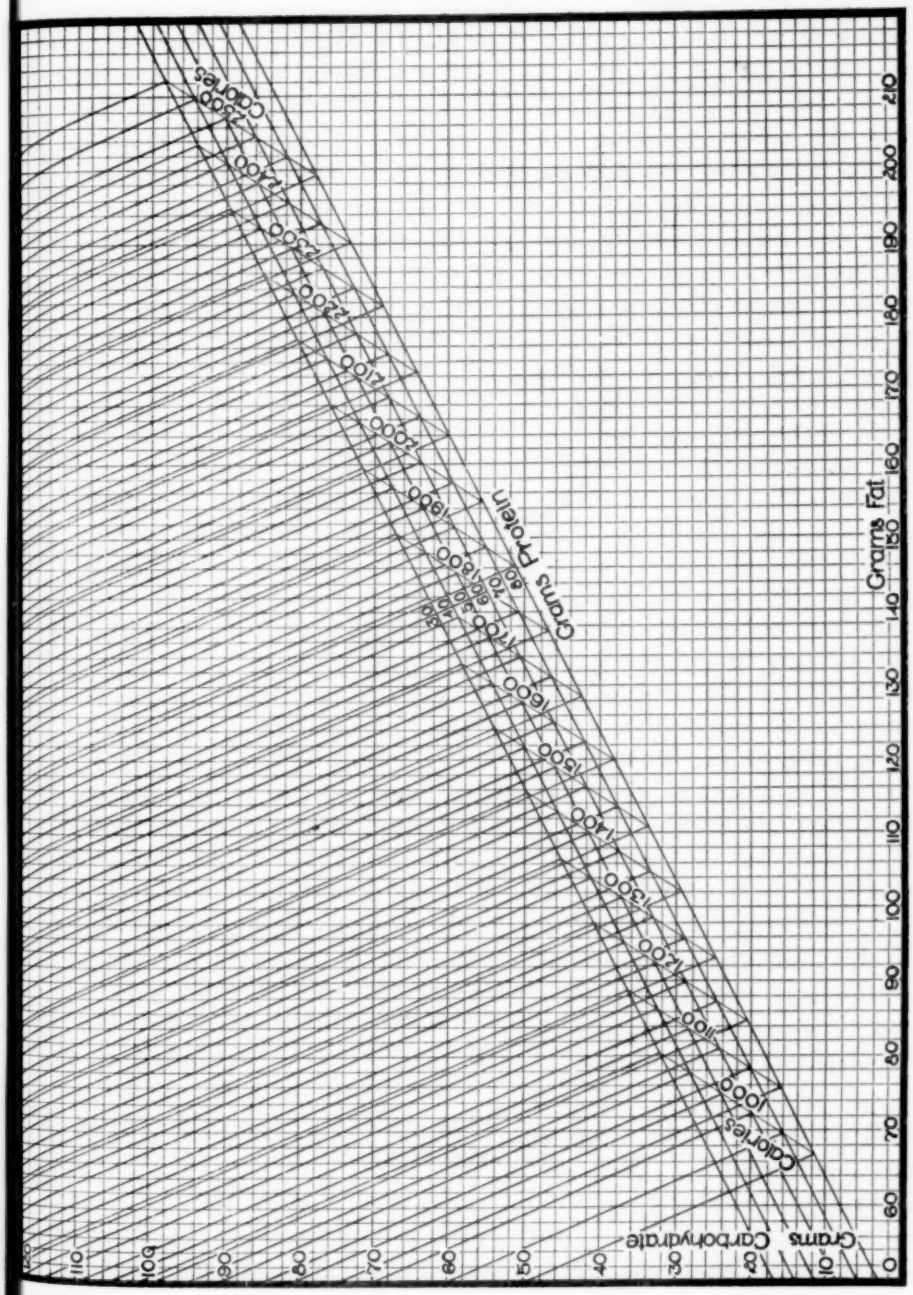

Chart 2.—Diabetic diet*. Identify the graph for the required number of grams of protein; run along it to the point where a member of the bank of graphs for the required number of calories rises from it; read off the coordinates of this point for the number of grams of fat and carbohydrate in the threshold diet; read off the coordinates of points higher up on this graph for diets of increasing carbohydrate; read off the coordinates of points along its projection beyond the intersection for diets of impending ketosis.

tion is outside the caloric equation. It occasions some further discrepancy between caloric intake and output.

Absorption is not equivalent to catabolism. Yet over a period of time a maintenance diet tends to become a replacement diet. Then ingestion and metabolizing correspond in the gross.

But they cannot agree in detail. The mixture is not completed and absorption does not proceed with the same time relationships for different foods. The absorbed derivatives of the several foodstuffs are independently distributed, accepted into the cells to be processes or loaded there, and remobilized or catabolized as required. Basal metabolism goes on without reference to absorption. The stimulative action of protein metabolites and the plethora effect of those of carbohydrate and fat alter the metabolizing mixture in different ways. Certain foodstuffs are preferentially metabolized in the availability of others. This situation is characteristically modified in diabetes. Not only is carbohydrate metabolism retarded and limited, but fat metabolism is inhibited and curtailed in favor of storage. Conversions among certain of the foodstuffs can occur. On such accounts it is most unlikely that there shall ever be a very close correspondence between the proportions of the several foodstuffs ingested and the proportions of the several foodstuffs metabolized. The only justification for calculating a dietic mixture with the purpose of establishing a metabolizing mixture is, that, although it ignores all the intermediary factors which may indifferently augment or cancel each other, it is still more conducive to the intended metabolizing mixture than any arbitrary diet is likely to be. Only on this basis is it feasible to prescribe a diet, which, if metabolized proportionately, would keep metabolism in a certain relationship to the threshold of ketosis.

No uniform metabolic mixture is in fact specific to the threshold of ketosis. Experimental findings[5] vary from the theoretical expectations of ketogenic-antiketogenic balance.[1, 2] But they do not establish any alternative ratio. Rather they plot the extent of deviation from the theoretical. The theoretical formulation remains the only definition available of the metabolic mixture at the threshold of ketosis.

The actual metabolizing mixture may be widely divergent from that of the threshold and still be safe from ketosis. The threshold must be drastically transgressed before any appreciable ketosis develops. Before the production of acetone bodies becomes quantitative there must be in the metabolizing mixture a large preponderance of ketogenic over antiketogenic molecules. When the production of acetone bodies finally comes up to the calculated expectancy it corresponds to the excess of ketogenic molecules over and above twice the antiketogenic molecules. Whereas the threshold ratio is 1:1, the stoichiometric ratio is $2:1^1$, to which corresponds the weight relationships of the equation

$$F=5\ CH+2.13\ F$$

So far is the formation of the first abnormal traces of the acetone bodies removed from their production according to the mass law.

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The Frequency and Clinical Manifestations of Intestinal Worms

By Paul F. Whitaker, M.D., F.A.C.P., *Kinston, N. C.*

In a former article the writer reported a series of five hundred stool examinations on consecutive patients presenting themselves for study. Since that time a routine stool examination has been continued, and the present paper embraces a series of 1650 cases. This work has been done to determine in a measure the frequency of intestinal parasitic infection in Eastern North Carolina. Some years back the subject was much before the profession, due to the work of the Rockefeller Foundation and enormous good was accomplished through this splendid work, particularly in discovering and treating hook worm infections. At that time one could stand on the street corner on Saturday afternoon in any North Carolina town and diagnose by inspection hook worm infection in the weazened, pasty, listless, and anhydremic faces of people from the rural districts. Now, however, this type of case is seldom seen, and unless the examiner is cognizant of the frequency of intestinal worms many cases are overlooked. It is apparently now a somewhat neglected subject.

The 1650 cases upon which this report is based were private white patients coming through the office or service of the writer at Memorial General Hospital, Kinston, N. C. No negro or child under twelve years of age is included in this series. These cases represent a fairly good cross section of the adult population, many infections being found in the homes of the well-to-do, as well as those in more moderate circumstances, and those from the rural districts. Out of the 1650 stool examinations made, 374 were positive, giving a percentage of 23 per cent infection with some form of intestinal worm. Of this number there were 347 cases of hook worm, 18 cases of round worm, three cases of dwarf tape worm, one case of pin worm, and three cases of beef tape worm. In the cases of beef tape worm the segments and not the ova were found in the stools. Of the total number it can be readily seen, that hook worm is by far the most prevalent parasite, with round worm next in order of frequency. Of the 18 cases of round worm, 8 of these were also infected with hook worm, and two of the three cases of dwarf tape worm also showed hook worm infection. Of the 374 positive cases 204 were males and 170 were females. The oldest positive case was that of a person 67 years of age, the youngest 12. While it is not thought that age is such a significant factor, this point is mentioned for the fact that we believe that the percentage of positive cases would

be ever greater in children than in our series of adult cases.

History and Symptomatology

A careful history will often lead one to suspect parasites. If asked directly the patient can often be made to recall having had dew poisoning, ground itch or foot itch in childhood or adolescence. Infection with hook worm is usually due to penetration of the unbroken skin by the larvae of the parasite. Sixty-two per cent of the positive hook worm cases gave a history of an eruption on the feet. This percentage would probably be higher if the patient's memory could go back far enough. Some patients can be made to recall having passed by bowel or even vomited so called stomach worms. All three of the cases of beef tape worm noticed the segments of the parasite in their stools. A voracious appetite is supposed to be a prominent symptom of tape worm, but none of these patients had this symptom. Sufferers with pin worm infection frequently complain of intense itching around the anus and vagina.

Weakness, dyspnea, and chronic and early fatigue were complained of by seventy-five percent of the positive cases. The greater the degree of associated anemia, the more marked were these symptoms. Nervousness, vertigo, anorexia, irritability, listlessness and headache are prominent symptoms. Vague digestive disturbances are quite common. We are greatly impressed with the frequency of intestinal worms in the so called neurotic or neurasthenic individual and we believe that this diagnosis will be made less often and with more caution if one will take the time and trouble to examine the stools. It is gratifying to see the results of treatment in this type of case.

Physical Examination

The appearance of the patient is often suggestive. The skin and visible mucus membranes are usually pale and suggest anemia. The patient is often but not always underweight. The muscles are usually flabby. In cases of pin worm infection the mucocutaneous junction around the anus and vagina is often reddened and hypertrophied from constant scratching. Slight edema of the ankles with bloating and purplish discoloration under the eyes, without cardiac or renal pathology is a fairly common finding. A mild icterus of the hemolytic type is sometimes present. Hemic murmurs were often found on cardiac auscultation in the more anemic cases. A palpable spleen is no uncommon finding. Thirty-eight per cent of the positive cases had a definitely palpable spleen. There were other patients in the positive series with palpable spleens, but they either had or gave a history of having had malaria, or some other condition that resulted in splenomegaly. These cases are not included in the thirty-eight percent reported. All cases with splenic enlargement had at least a moderate secondary anemia. Why almost forty percent of patients with intestinal worms should have an enlarged spleen is an interesting question. It might be explained as follows: One of the functions of the spleen is to remove crippled or worn out erythrocytes from the circulation. The parasites certainly produce anemia probably by elaborat-

ing a hemolytic substance, which acts on the red blood cells. Granting that this theory is correct the cells rendered useless by the action of the elaborated toxin are removed from the circulation by the spleen in such numbers as to cause splenic enlargement.

Laboratory Examination

In no condition is accurate and properly interpreted blood and stool examinations of more value than in the diagnosis of intestinal worms. The differential blood count revealing an increase in eosinophiles is of inestimable value in leading one to suspect intestinal parasites. Eosinophilia of from 3 to 15 percent is practically a constant finding in hook worm and tape worm infection. Contrary to some observers we believe it to be present in ascaris infection as well. The highest eosinophile count in any case was 15 percent, the lowest 3 percent. The average eosinophile count for the whole series was 5.75 percent.

Every patient with intestinal worms in our series save two had a secondary anemia, characterized by a diminution of red blood cells and hemoglobin. The highest red cell count in any male was 5,020,000, the lowest was 1,340,000; the average was 4,531,000. The highest hemoglobin percentage was 90, the lowest 35; giving an average of 72.6 percent. The highest red cell count in any female patient was 4,360,000, the lowest was 1,000,000, giving an average of 4,140,000. The highest hemoglobin percentage in any female case was 80; the lowest 18; giving an average of 66.3%. Accepting 5,000,000 red blood cells per cubic millimeter of blood as normal in the male, and 4,500,000 as normal in the female with normal hemoglobin percentage as 90 and 80 respectively, there can readily be seen the degree of anemia produced. The presence of eosinophilia in intestinal parasitic disease is interesting. According to Neal and Robnett, eosinophiles are not only present in the blood of patients with intestinal parasitic disease, but are present also in the wall of the intestine. Their presence, like the presence of polymorphonuclear leucocytes in inflammatory disease, and lymphocytes in tuberculosis and syphilis, is intimately bound up in chemotaxis, specific and selective action of the cells for particular irritant micro-organisms and their toxins, and as a response to the need to build up protective antibodies, local enzymes and ferments.

The recognition of the ova of the parasite in question in the stools is of course the final procedure upon which a diagnosis is made. The technique of the stool examination of these cases is as follows: A small particle of the stool is mixed with tap water and shaken vigorously. It is then centrifuged for one minute and the supernatant fluid poured off. Tap water is again added and the mixture centrifuged for one minute. The ova are concentrated in the bottom of the tube, and this material is examined under the microscope. It requires training, skill, and patience to recognize and differentiate the various ova, and this work should be done by one meeting the requirements. Examination of the fecal mass with the naked eye will suffice for the pinworm. Each parasite is about a quarter of an inch in length, colorless, and projects its extremity above the

fecal mass where it moves about slowly like threads waving in the air. A negative stool examination, however, should not deter one from making the diagnosis of hookworm infection where eosinophilia is present, and the symptoms warrant the diagnosis. We have repeatedly demonstrated the presence of ova in the stools after treatment of such cases.

Treatment

For hookworm and round worm infections a combination of oil of chenopodium and carbon tetrachloride is used in average doses of 30 minims each put up fresh in capsules. This dose is varied in some cases, depending upon the condition of the patient.

For tapeworm infections we have found nothing better than the oleoresin of aspidium in 40 grain doses combined with two drams of spirits of chloroform. Proper purgation of the patient with abstinence from food is essential.

For pinworm infections quassia enemas are used. It takes prolonged and persistent treatment to rid the patient of this troublesome parasite. We treat the patient until a negative stool is obtained, and have found that it takes an average of two treatments to effect a cure.

The treatment of deRivas of Philadelphia is mentioned. He treats a patient by the instillation of physiologic saline solution into the duodenum and rectum, basing his treatment on the assumption that a solution at a temperature of from 45 to 47 degrees centigrade is lethal to the parasite, and at the same time has no ill effect on the intestional mucosa. Experimental work on animals tends to bear out his assumption. The author has had no experience with this method, but it is quite a common clinical observation that roundworms are often vomited by children with hyperpyrexia, the high temperature probably playing a part in causing the parasite to leave its host.

Summary and Conclusions

1. Intestinal parasitic disease, particularly hookworm infection, is much more prevalent than is generally recognized and by no means so easily eradicated as is commonly supposed.

2. We believe that careful histories, thorough physical examinations, carefully made stool and blood examinations, with their proper interpretations, offer the best means of detecting these infections.

3. Quite a number of so-called functional nervous patients suffer from unrecognized intestinal parasitic infections, and respond promptly to treatment.

4. A palpable spleen is recorded as a common physical finding in intestinal parasitic disease and the explanation of this finding is attempted. So far as we know, this finding has not before been reported as associated with intestinal parasites.

5. Secondary anemia is practically a constant finding in intestinal parasitic disease. Attention is again called to increase of eosinophiles.

6. Treatment of the various parasites is discussed. Treatment is persisted in until a negative stool is obtained, and it has been our experience that it takes an average of two treatments to effect a cure.

7. In conclusion I wish to thank Miss Mildred Ringle, R. N., technician

at Memorial General Hospital, Kinston, N. C., for her assistance in studying these cases from the laboratory standpoint. Her enthusiastic and accurate work has illuminated the study of these cases.

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Plasmochin As An Aid in Malaria Prevention*

By Neil P. McPhail, M.D., *Puerto Barrios, Guatemala*

DURING the twenty-two years in which the Medical Department of the United Fruit Company has made earnest efforts to reduce the incidence of malaria in the Motagua Valley where they operate, dependence was placed for the first number of years on two main measures.

On one hand all collections of water in close proximity to campus were drained when possible, and treated with oil or Paris Green when drainage was impractical. These measures were directed against the breeding of the Anopheles mosquito. On the other hand the human carrier was treated with lengthy courses of quinine, arsenic, and other tonic preparations, under as close supervision as possible.

By experience we found that these measures reduced the incidence of malaria very much, and a smaller number of employees developed serious forms of malaria, requiring hospital treatment, and the death rate was much reduced.

In the later years, about 1925 and 1926, when the thick film method of blood examinations was perfected, and in general use, we began extensive blood surveys of the camp labourers and their dependents. A surprising number of those bloods were found to contain gametocytes, frequently when no trophozoits (ring forms) could be demonstrated.

We then began to examine the bloods of patients about to be discharged from the hospital, in a convalescent state after malaria attacks. We found that an alarming number of those, whose symptoms of fever had disappeared for a minimum of five days, who had excellent appetites, and were demanding to be discharged, carried large quantities of gametocytes in their peripheral blood. This presented a difficult problem, as we found it impossible to clean the sexual forms from the blood by quinine and arsenic treatment in a reasonable time. It meant that we were discharging large numbers of convalescent patients from the hospital, to go back to their camps, to join the ranks of many already there, all in an excellent state to infect mosquitoes.

About this time we had the first opportunity to test the value of plasmochin in the treatment of malaria.

A large series of hospital cases of malaria were placed on plasmochin treatment, and daily blood specimens taken and examined.

The dosage recommended by the manufacturers and sponsors of plasmochin was 9 to 12 centigrams daily

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for six days, and we began with that dose.

All cases chosen had positive bloods on admission, and a series were given plasmochin alone, and another series were given plasmochin and quinine together. The most interesting and important development was that in all the cases, in a series of over 100, gametocytes had entirely disappeared from the peripheral blood in five days, and in the majority of cases on or before the fourth day.

Another notable finding was that in cases of estivoautumnal infection the ring forms did not disappear so quickly in those treated with plasmochin alone as in those in which quinine was combined with it.

I will not detail all experimental work carried out, but when we had checked carefully over 1000 cases, we had come to the following conclusion:

(1) Plasmochin had a much more powerful effect in destroying the gametocytes of all forms of malaria than any treatment which we had previously known.

(2) Quinine was much more effective in the destruction of ring forms of aestivoautumnal malaria (trophozoites) than plasmochin.

(3) The ideal treatment in all types of malaria infections was a combination of plasmochin and quinine. With this treatment symptoms were rapidly controlled, the formation of gametocytes effectively prevented, and already existing trophozoites and gametocytes were rapidly destroyed.

The results made it apparent that at last we were able to discharge convalescent malaria cases from hospital with their peripheral blood free from sexual forms of parasites. In this way we felt we had arrived at another milepost of progress, and returned all hospital cases to their camps unable to infect mosquitoes.

During above experiments we found a small percentage of the cases develop signs of toxicity, before completion of the course. The main symptoms were pain in the abdomen, cyanosis of lips and nails, and occasional nausea. Less than 5% of the patients developed this condition, and all promptly recovered when treatment was suspended. The dosage for adults had been 2 grm. of quinine and 9 centigrams of plasmochin for five days. On account of toxic symptoms occasionally developing we felt that plasmochin, while a valuable aid in hospital treatment, could not be utilized as an aid in field-work, in the dosage recommended.

We undertook a series of treatments, where we gave 6 centigrams of plasmochin instead of 9, and controlled results with daily blood slides.

We were gratified to find that the smaller dose gave identical results with the larger. In a large series of cases we noted that toxic symptoms were practically absent, and we felt justified in believing that we could safely introduce plasmochin, in these reduced doses, to our field work.

Later still (1928) we experimented along similar lines in hospital with a dosage of 3 centigrams daily for six days, combined with two grams of quinine, and careful blood control examination showed that gametocytes disappeared in 4 to 5 days at most. With this dosage we found toxic symptoms were unknown.

At this stage we decided that plasmochin could safely be added to our field dispensary and overseers, stocks of medicines, for use in this dosage, to light cases of malaria who did not wish to come to hospital.

At intervals blood surveys are made of all the inmates of our camps, and a list of the positive ones submitted to the overseers. All adults on the list receive 2 grams of quinine and 3 centigrams of plasmochin daily, in 2 doses, for six full days, and children's dosage is worked out according to age and noted on the list.

In earlier surveys we checked up all the bloods of those treated, the day after treatment was completed. Results were so uniform, and negative bloods so constant, that we have practically discontinued a second examination and so save the doctors and technician's time. The re-surveys left no doubt at all that the treatment had cleared the peripheral blood of parasites—rings and gametocytes—and for the time being all individuals were unable to infect mosquitoes.

When blood surveys were made in camps before we had plasmochin, and treatment given to positives with quinine and arsenic, we found in the re-survey, that in most cases ring forms had disappeared but that we frequently found more sexual forms present in the peripheral blood than we did before treatment. As long as sporulation continues in a malaria attack gametocytes will almost certainly develop, and quinine is unable to prevent this formation, as plasmochin does.

With plasmochin at our disposal we have an excellent aid in the prevention of mosquito infection, a safe and valuable help in anti-malaria work in the camps.

We have learned from experience that we cannot eradicate malaria from large tracts of tropical low-lying lands, such as those occupied by the plantations of the United Fruit Company, with anti-mosquito measures alone.

The treatment of the human carrier is a most important measure in any campaign for the reduction, and ultimate eradication, of malaria in a large and scattered community.

I have outlined above one of the methods which we have found most useful in attacking the infections carried by the human being, viz., periodic surveys, with rigidly supervised treatment of those with positive bloods. I might add that our practice has been to treat *all inmates* of any camp in which inhabitants are found to be more than 30% positive. This measure has been extremely useful, and has had no resistance from the labourers or their dependents, who now understand that we are trying to help them. It is over two years since we have had to adopt this measure, as we have not had a community show up with 30% infection in that period.

Another camp measure which I believe to be our most valuable aid to the reduction of mosquito infection is in the rigid daily round of each room in each camp in the Division by an intelligent administrator or practicante. Repeated medical surveys of employes in the Motagua Valley make it certain that 85 to 90% of all those feeling ill owe their indisposition to malaria infection. When a man, woman or child feels ill he is seen in less than 24 hours after getting ill.

Appropriate early treatment with a cathartic, quinine and plasmochin not only prevents the individual from becoming worse, with consequent loss of time and a probable serious case of malaria, but it prevents him becoming a reservoir of infection to the mosquito.

Some skilled observers have more recently undertaken a study to determine the minimum useful dose of plasmochin, as regards prevention of mosquito infection from human beings heavily loaded with gametocytes in their periferal blood.

Professors Barber and Kemp who studied malaria conditions in the Motagua Valley some years ago, and Col. Whitmore, working in different sections of the Tropics reached the same conclusions, which are of extreme interest to those of us engaged in preventive work. They determined that a dose of 2 centigrams of plasmochin so devitalized the gametocytes in a heavily infected human being that the mosquitoes which were liberally fed on his blood were unable to develop oocysts.

When such highly experienced and careful observers are willing to make such a statement I feel doubly sure that we have in plasmochin an ally of vital importance in our fight to reduce, and finally eliminate, malaria from the low-lying portions of Guatemala.

Up to the present we have used in our work in Quirigua 1,388,000 tablets of plasmochin and feel justified in coming to the following conclusions concerning the use of plasmochin in malaria.

(1) Plasmochin effectively destroys the gametocytes of all forms of malaria when given in doses of 3 to 4 centigrams daily for one week.

(2) Combined with quinine plasmochin is a safe and sure way of preventing formation of gametocytes during an acute attack of malaria, and the combination destroys all types of parasites.

(3) Toxic symptoms need not be dreaded when dosage is limited to 3 centigrams daily for a week or more.

(4) We have ample clinical proof to substantiate a tentative statement that plasmochin is of importance as a curative factor in chronic cases which have resisted long efforts at eradication with quinine and arsenical preparations.

(5) Plasmochin is a valuable aid, in the hands of a competent sanitarian, to the diminution of mosquito infection, through the undoubted properties which it possesses of causing the devitalization and destruction of malaria gametocytes.

Editorial

TOBACCO PATHOLOGY

That there has been a great increase in clinical disturbances ascribed to tobacco smoking during the last decade would appear from the increasing frequency in the literature of articles dealing therewith. Particularly in Germany have numerous articles dealing with this subject appeared. Since 1922, Kűlbs, Hofstätter, Deneke, Fűrbringer, Morawitz, Leschke, Kuttner, Frank, and others have published contributions to our knowledge of the clinical conditions due to excessive smoking. In 1924, Hofsätter's monograph on "Rauchende Frau" appeared in Vienna. Kűlbs reported observations on 456 cases in which definite conditions were ascribed to excessive tobacco smoking. One writer speaks of the increasing smoking-madness, which particularly in the case of women smokers, is bringing an increasing number of patients into the German Polyclinics, whose symptoms are shown to be due to excessive smoking, because they disappear when the patients refrain from smoking, and reappear when smoking is resumed. Much of this Polyclinic material is made up of young individuals, particularly of young women. The great majority of these cases complain of nervous cardiac conditions, neuralgias, emaciation, gastric disturbances with symptoms resembling those of gastric ulcer, sexual disturbances, pains in the lower extremities, etc. That these conditions vary so greatly in different individuals is easily explainable by individual differences in localized lowered resistance and in the individual differences in tolerances. Some German clinicians, as Lippmann of Hamburg, believe that the harmfulness of tobacco smoking is much under-rated, inasmuch as the symptoms usually disappear under abstinence from tobacco. He advises that in vague and doubtful cases the possibility of tobacco etiology should be borne in mind. Lippmann (Klin. Wchschr., January, 1931, p. 169) discusses the rarer forms of tobacco injury, considering first the effects upon the heart. He is convinced that tobacco has an elective spastic action on the peripheral vessels, and on the coronaries. Angina in smokers is not rare. Kűlbs found that 13 per cent of his tobacco patients suffered from angina pectoris. Tobacco angina due to spastic coronary contraction affects younger individuals more often than angina due to coronary sclerosis. It has also a more favorable prognosis as it will not occur again if the individual abstains from smoking. Hypertonus and tobacco injury bear no well-defined clinical relation to each other; but a high blood pressure in young individuals may be produced by tobacco. The vascular spasms typical of tobacco poisoning are often the cause of pains in the extremities, which since

Cracot and Erb, have been known as "intermittent limping." Parasthesias and cramps in arms and legs, and also in the head, diffuse or sharply localized, are often seen to disappear by complete abstinence from tobacco. This may be taken as proof of their tobacco etiology. In severe forms endarteritis may be found, but in the milder forms in which the spastic nature is certain, there is rapid relief from the pains, with normal pulse and normal vessels, through abstinence. Intestinal symptoms, due to vagus stimulation, such as constipation, intestinal and stomach cramps, are very common in young smokers. A goodly number of ulcer patients are strong smokers; but many cases suspected to be peptic ulcer disclose themselves finally as tobacco cases. In these cases we often see increase of the symptoms suggesting the picture of a tabetic crisis. These symptoms disappear during periods of abstinence to return when the patient resumes smoking. Cases of gastrosuccorhea may have a neurogenous origin due to tobacco. The more rare forms of tobacco symptoms in the form of coronary spasm, optic atrophy, intermittent limping, acoustic neuritis, gastrosuccorhea, etc., may occur singly or combined in different cases, according to the lowered local resistance and the individual degree of tolerance. Particularly in the case of young women smokers (college girls) does there appear to be a great increase in the occurrence of vague neuralgias and gastrointestinal symptoms. It is well for the practitioner if he develop a suspicious attitude towards the habit of smoking, if it is present, in such patients. An enforced abstinence will sometimes produce striking cures. Many of our clinicians, confirmed smokers themselves, do not readily suspect the, to them, harmless habit, of being at the bottom of such symptoms; and so fail to benefit their patients. As to the relationship of smoking to cancer of mouth, esophagus, throat, larynx, and lungs, all authorities agree that smoking habits undoubtedly increase the liability to these forms of cancer. Other factors, such as infection, poor dental conditions, burns, mechanical iritation, enter into the production of smoker's cancer. Hoffman believes that the increase in cancer of the lungs throughout the civilized world, is, in all probability, to a certain extent directly traceable to the more common practice of cigarette smoking and the inhalation of cigarette smoke. The latter practice, he believes, unquestionably increases the danger of cancer development. It is still too soon to tell whether the recently acquired smoking habits of women will lead to an increase in the incidence of lip, throat, esophageal, laryngeal, and pulmonary cancer in the female sex; but such an increase appears to be not unlikely.

HAS THE TONSIL AN INTERNAL SECRETION?

At last, the tonsils, those small organs that to many clinicians seem not only useless but positively dangerous, and made apparently only to furnish employment for their removal, seem to be acquiring a new importance in the minds of some of the continental physicians. That the tonsils are primarily defence organs, even the most ardent believer in tonsillectomy will admit. The function of its lymphoid tissue is

to destroy the bacteria entering through the crypt and surface epithelium. A catarrh of the mucosa leads to a hyperplasia of the lymphatic tissue. The increasing resistance or immunity of the mucosa with advancing age leads to an inactivity atrophy on the part of the lymphoid tissue. Halasz reports eighteen cases of chronic pharyngitis developing in patients after tonsillectomy. The blood picture of these patients showed a leucopenia with a relative lymphocytosis. These patients were given subcutaneous injections of an albumin-free tonsil-extract, made from calves' tonsils. The injections were given daily, in doses of 1 cc. (extract of 1 gram of gland). One patient received 12 injections, the other fewer. After the first 1-2 injections the leucopenia was transformed into a leucocytosis, but the lymphocytosis remained more or less unchanged. In all eighteen patients the pharyngeal catarrh was promptly healed. Therefore, it might be regarded as a "pharyngitis tonsillo-priva" due to the lack in the organism of the product of the removed tonsils. Here is an opportunity for the development of a new therapeutic field, or fad.

THE IODINE-DEFICIENCY THEORY OF GOITER

Johann Holst of Oslo, referring to Hellwig's recent paper in the Klinische Wochenschrift, in which the latter mentions the frequent occurrence of goiter in the iodine-rich region of Danzig, goes on to say, that in Norway goiters are also seen which are surely not caused by a lack of iodine. Particularly is this the case in young girls in Oslo, where in general, large amounts of iodine are excreted in the urine. Recently he and a number of his colleagues investigated a small endemic of goiter on the west coast of Norway, in a region where there was no lack of iodine. In the case of these goiters, iodine had no prophylactic effect, because iodine deficiency was *not* the cause of these goiters. Nevertheless, the fact that endemic goiter not due to iodine deficiency occurs should not be taken as proof, as Hellwig and Liek appear to think, that the theory of iodine deficiency is false. It only goes to show that there are other strumogenous factors than iodine deficiency. One may find in a given region one cause of goiter to be active, while in another region another cause may be present. By far the most common cause of goiter in Norway is iodine deficiency. The nature of the other causes of endemic goiter, we do not know. Since we know that in animal experimentation different forms of deficient or one-sided nutrition can produce changes in the thyroid, it follows that other causes of goiter are probably dependent upon nutritional factors.

ALCOHOL AND POSTERITY

A. Bluhm of Munich has contributed a noteworthy experimental study on the blastophthoric effect of alcohol, which confirms Stockard's experiments with alcohol in this country, as well as those of Weller as to the effect of lead poisoning on the progeny of successive generations. Bluhm concerned herself with the problem whether parental alcoholism produces changes in the posterity that are in a strict sense hereditary, or whether the blasto-

phthoria produced by alcohol is only temporary, disappearing in the course of a number of generations. The experiments were carried out on white mice; 32,300 individuals were employed. Only the males of the first generation were treated by means of alcoholic injections under the skin of the back. These animals received six times a week injections of 0.2 cc. of a fifteen per cent alcoholic solution. The method had previously been tried out in experiments lasting three-quarters of a year. Applied to man this amount of alcohol employed would amount to a daily consumption of 105 cc. of alcohol for an individual of 70 kg. The first generation consisted of 114 pairs of experimental animals and 114 pairs of control animals. Their progeny were paired in closest incest, and bred to the eighth filial generation. The food consisted of a standardized, abundant diet, with all of the food element well balanced. The investigation concerned itself with the following factors: duration of life, growth, fertility, malformation, and degeneration. The results of the observations were as follows: The prenatal mortality of the posterity was up to the 7th generation signifying higher than in the controls. The progeny of a normal control female and an alcoholic male were shown to have a much less chance of surviving the nursling period than had the progeny of an alcoholic daughter and a normal control son. The same was true for the crossings of uncle, great-uncle, and great-great-uncle. The alcoholism of the great parent prevented a part of the progeny from reaching the age of fertility and led in the higher ages to a significantly lowered resistance against death. The growth was slightly affected in the male descendants. Paternal alcoholism was able to produce sterility even in members of the seventh filial generation. The increased mortality in the new-born of the descendents of the alcoholic lines is dependent in the first place upon an injury to the genes, which must have its seat in the sex-chromosomes. It is regarded as a defence reaction, which the sperm, damaged by alcohol, excites in the egg, and which in the course of generations leads to an increase of the defence material. Intestinal catarrh played a important rôle in the cause of death. In regard to the occurrence of malformations and degenerations in the alcoholic posterity no difference was noted from that in the control posterity, except for a marked general stunting of the alcoholic posterity. In favor of the genetic significance is the much more frequent involvement of the male descendents, which appear to be the exclusive carriers of the alcohol damage. The importance of this work of Bluhm can hardly be over-estimated. It is the first experimental work in blastophthoria in which proof is offered of direct involvement of the genes or chromosomes, and a definite localization of the injury in the sex-chromosomes. This is, therefore, added experimental proof of the transmission of acquired pathological characters; and has, therefore, most important biologic and eugenic significance.

Abstracts

Mercurialism Due to External Use of Mercurochrome. By D. E. H. CLEVELAND (Can. Assoc. Med. Jour., Feb., 1931, p. 272).

Most of the adverse reports concerning the use of mercurochrome refer to its intravenous use. A number of reports have been published of mercurial intoxication from intravenous use and also from its application to cavities lined with mucous membrane. Mercurial dermatitis caused by its application to skin surfaces, as is sometimes observed in connection with the use of white precipitate ointment or bichloride lotions, is also known to occur, but few if any cases have been reported of general mercurialism resulting from its use on the skin. Cleveland reports a case showing that the use of mercurochrome as a skin disinfectant is not without dangerous possibilities. In a newborn child, apparently otherwise healthy, the lesions of impetigo contagiosa were treated over a period of 12 days with 4 per cent mercurochrome. About the 7th or 8th day the child began to be salivated, failed to feed properly, and lost weight, apparently due to soreness of the mouth, and on the 11th day developed a generalized erythema. Albumin was found in the urine. All these symptoms subsided rapidly upon withdrawing the mercurochrome. Two months later the child was reported by the mother as being perfectly well. Cleveland regarded the case as one of mercurialism due to the external use of mercurochrome.

Meningitis During Convalescence from Varicella. By LAIGNEL-LAVASTINE, MIGET and CONSTANTINESCU (Bull. et Mem. Soc. Med. des Hôp. de Paris, October, 1930, p. 1448).

Meningeal reactions have been frequently reported as occurring in varicella; but the case reported here is believed to be the first case recorded in which a fatal meningitis occurred in convalescence from varicella. The patient was a young man, aged 18, who had apparently a mild attack of varicella. While convalescing from this attack, he developed symptoms of a severe meningitis, with convulsions. Death occurred on the fifth day. The autopsy showed a diffuse purulent leptomeningitis with involvement of the cortex. Tuberculosis was excluded by the bacteriological examination and by the inoculation of guinea pigs, both of which were negative. No other source of the meningitis was found, and the authors look upon it as directly connected with the varicella. Meningitis must, therefore, be regarded as a possible, though rare, complication of varicella.

Certain Aspects of the Pathogenesis of Angina Pectoris. By J. H. MEANS (Can. Med. Assoc. Jour., Feb., 1931, p. 193).

It is important to bear in mind that the term, angina pectoris, denotes a symptom and not a disease. Its distinguishing features are its paroxysmal incidence, its location in the breast (substernal, more to the left than the right), its relation to effort, and its tendency to end in sudden death. To these may be added as a further essential quality, prompt relief by drugs of the nitrite group. In fact, in doubtful cases, this therapeutic test may be considered the final diagnostic proof (questioned by Herrick). Of pains in the region of the heart which are not to be regarded as angina pectoris, the more important are "fatigue" pain, which is dull aching, or sometimes stabbing, usually over the heart itself. Such pain occurs in a variety of conditions, in young people with neurocirculatory asthenia, in certain persons unduly sensitive to tobacco, in organic diseases of the haert, as in mitral stenosis, and hypertension. Presumably it is evidence of myocardial protest, whether the heart is being driven excessively by nervous stimulation or

by the handicap of organic cardiovascular disease. It differs from true angina in location, incidence, relation to effort, and response to drugs. When occurring in connection with organic cardiovascular disease, at least, it responds to digitalis rather than to nitroglycerine. There is also pain in certain cases of pericarditis and aneurysm, clearly very different from angina pectoris. Then there is the pain of cardiac infarction, which Means regards as essentially the symptom of angina pectoris continued beyond its usually paroxysmal duration and accompanied by other manifestations which the infarction brings about. In other words, instead of attempting to distinguish between cardiac infarct and angina pectoris as two separate diseases, we shall do better if we say that in cardiac infarction angina pectoris of a peculiarly continued sort is a prominent symptom; but the symptom angina often occurs with no infarction of the heart. The theories in regard to angina fall into two main groups—that of its coronary origin and that of its aortic origin. The former is the older and more likely correct view. In the light of present knowledge the latter might almost be dismissed. The coronary theories of angina pectoris center about transient asphyxia of the heart. A spasm of the vessels has been supposed to deprive the myocardium temporarily of an adequate supply of blood (ischemia). That spasm of the coronaries can take place in man has never been proved. Keefer and Resnik have advanced the hypothesis that anoxemia can come about merely through a disproportion between the demands upon the heart and its oxygen supply. If because of suddenly increased work the myocardium needs more oxygen, and the coronaries do not allow it to get it, anoxemia may result even in the absence of any spasm. A similar view has probably been in the minds of other writers who have noted the relation of general metabolic level to the incidence of angina, particularly in cases with over- or under-function of the thyroid. Means would like to use the phraseology that the symptom angina pectoris is evidence of insufficient coronary flow. This state of relativity involves a variety of presumably independent variables, anything that causes a disturbance in balance between the work the heart has to do and its coronary supply. Means is inclined to agree with Keefer and Resnik that anoxemia is the more likely cause. His conception of relative insufficiency of the coronary flow is best illustrated clinically in anemia and in thyroid disease. The occurrence of angina pectoris in patients with severe anemia is well known. The degree of anemia bears no relation to the incidence of angina among different persons; but if the theory of a relative insufficiency of coronary flow is correct, a close relationship between the occurrence of attacks of angina and the level of the hemoglobin in any given individual should be found. Means cites a case proving this point. In the field of thyroid disease angina is met under two sets of circumstnaces. First, pain having the classical characteristics of angina may occur in thyrotoxicosis, and disappear after its abolition. He regards this as bearing out the principle of relative insufficient coronary flow, and cites a case to illustrate. The other thyroid situation in which angina may occur is that of myxedema, when thyroid is administered in too large doses. The application of the principle of relative insufficiency of the coronary flow is the same as in thyrotoxicosis. Caution should be exercised against thyroid overfeeding. Another instance of angina pectoris developing as a result of elevation of metabolic rate induced by the administration of a calorigenic hormone is that produced in the case of epinephrine. The increase in metabolism after epinephrine injections takes place at once and reaches its peak in from 20-40 minutes. The average time required for the development of angina coincides after injection of epinephrine fairly closely with the peak of the calorigenic curve. The pain comes on at the time of greatest metabolic demand. Epinephrine also greatly increases the work of the heart. It is small wonder, then, that epinephrine will produce angina in those whose coronaries are less elastic than they once were. Means doubts the propriety of using injections of epinephrine as a diagnostic test in doubtful cases of angina, as suggested by Levine and his co-workers. He regards it as safer to wait for a spontaneous attack and then follow the old custom of observing whether

nitroglycerine will give relief. A totally different but also important aspect of the pathogenesis of angina pectoris lies in the threshold of sensitivity to pain. Individuals vary greatly in this respect. Such variations certainly playe a rôle in determining the occurrence of the symptom angina. The difference between colored and white races is pointed out. Means then discusses the neurology of the pain in angina, and the recent theories as to its origin. As to the treatment of angina, when metabolic or hemodynamic factors are present, these can be corrected. In general, it is important to keep the demand upon the coronaries, from the point of view of work performed, within the limit they can stand, but it is equally important to recall and treat the emotional factors which may play a very vital rôle. The psycho-therapy of angina, which may be of a very simple sort, reassurance, encouragement to the patient to do as much as he can within his limit, is a very essential part. The new treatment by sympathetic block, Means believes, is indicated only when attacks are so frequent and severe that the handicap is great.

Sudden Cardiac Death from Ventricular Fibrillation and Its Treatment. By G. W. PARADE. (Zeit. klin. Med., 1930, p. 641.)

The symptoms of ventricular fibrillation express themselves in the triad of the sudden onset of symptoms leading to death after a few seconds, with persistence of the respiration. The causes of ventricular fibrillation are: electric currents, fear, coronary spasm, sudden increase of blood-pressure in bath, chloroform, digitalis, strophantin, adrenalin, morphine, caffeine, ether, air-embolism, embolism, thrombosis of coronary arteries, infectious-toxic damage of myocardium by diphtheria, typhoid fever, scarlet fever, rheumatic fever, syphilis, Chagas' disease, and angina pectoris. In all cases of cardiac damage following any of these causes, it is important to use cardiazol, quinidin intravenously, heart massage, and artificial respiration. For the prevention of the condition, safe-guarding and protection from all of these causes, and eventually quinidin, are indicated.

Studies on the Etiology of Rheumatoid Arthritis. I. Bacteriological Investigations on Blood, Synovial Fluid, and Subcutaneous Nodules in Rreumatoid Arthritis. By M. H. DAWSON, MIRIAM OLMSTEAD, and R. H. BOOTS (Proc. of the Soc. f. Exper. Biol. and Med., January, 1931, p. 419).

The clinical evidence pointing to an infective origin of rheumatoid arthritis has led numerous investigators to seek a bacterial agent to which etiological significance could be ascribed. A great variety of such agents has been reported, but lack of uniformity in the results obtained has confused the issue. Cecil, Nicholls, and Stainsby, by the use of a special technique, claim to have demonstrated the presence of streptococci in the blood stream in 61.5 per cent of a series of 78 cases examined. Because of the unusual nature of this report and the importance of their findings, the present investigation was undertaken. The greatest care was exercised to follow their technique. The patients selected in all cases presented the characteristic clinical syndrome of rheumatoid arthritis. Cases of hypertrophic and degenerative osteoarthritis were not included. One hundred and five separate blood cultures were done on 80 patients. Repeated blood cultures were done on selected cases. 31 samples of blood were obtained from 16 normal individuals and subjected to similar methods of culture, for control. The results may be summarized as follows: In spite of the greatest care to conduct all manipulations under sterile precautions the technique was so involved as to call into serious question the significance of all bacterial growth encountered. Blood cultures on patients suffering from rheumatoid arthritis failed to yield results which could be considered of etiological significance. No essential difference was found in the variety and character of the bacteria encountered during the culture of specimens of blood from patients with rheumatoid arthritis and of the control material. On two occasions colonies of *Streptococcus viridans* appeared during the culture of specimens of sterile agar subjected to similar manipulations. Twenty-three samples of synovial fluid, obtained from 19 patients suffering from rheumatoid arthritis were cultured both aerobically and anaerobi-

cally on a great variety of media. The cultures failed to yield organisms which could be considered of etiological significance. Careful bacteriologic studies were carried out on a series of 16 subcutaneous nodules from 11 patients suffering with rheumatoid arthritis. Aerobic and anaerobic cultures of these nodules in a wide variety of media failed to yield organisms which could be considered of etiological significance.

Studies on the Etiology of Rheumatoid Arthritis. II. Agglutination Reactions with Hemolytic Streptococci in Rheumatoid Arthritis. By M. H. DAWSON, MIRIAM OLMSTEAD, and R. H. BOOTS (Proc. of Soc. f. Exper. Biol. and Med., January, 1931, p. 421).

The bacteriological investigations on the blood, synovial fluid and subcutaneous nodules in rheumatoid arthritis reported by those investigators entirely failed to confirm the results reported by Cecil, Nicholls, and Stainsby. The latter had, however, further reported that the sera of patients suffering from rheumatoid arthritis possessed the property of agglutinating their "typical strains" to a remarkably high titre. Through the courtesy of Dr. Cecil several "typical strains" were made available. Specimens of serum were obtained from a large number of patients suffering from rheumatoid arthritis and agglutination tests were done using these strains as agglutinogens. For control purposes a large number of other organisms obtained from a variety of sources was similarly employed against the sera of patients with rheumatoid arthritis. The study was further controlled by utilizing a large number of specimens of serum obtained from patients suffering from both related and unrelated diseases. In addition to the "typical strains" of Cecil, Nicholls, and Stainsby, which, in the authors' experience showed varying degrees of hemolytic properties, cultures of *Streptococcus hemolyticus*, 4 strains including those from scarlet fever, erysipelas, and obtained from the throat of a patient with rheumatic fever; *Streptococcus viridans*, 7 strains; *Streptococcus anhemolyticus*, 12 strains; green diplococci (undertermined), 3 strains; and *Staphylococci, 5 strains.* Specimens of sera obtained from 66 patients suffering from typical rheumatoid arthritis were employed during the course of this study. Control sera were obtained from 50 cases of both related and unrelated diseases. The results of over 1,000 agglutination tests, using 37 different cultures as agglutinogens on 66 cases of rheumatoid arthritis and 50 control cases have led to the following conclusions: In the great majority of cases sera of patients with rheumatoid arthritis possess the property of agglutinating hemolytic streptococci to an extraordinarily high titre. Strains of *Streptococcus hemolyticus* obtained from scarlet fever, erysipelas, and from the throat of a patient with rheumatic fever were agglutinated by these sera to as high a titre as were the "typical strains" of Cecil, Nicholls, and Stainsby. Absorption tests carried out with *Streptococcus hemolyticus* from scarlet fever, erysipelas and the "typical strains" of Cecil, Nicholls, and Stainsby, failed to show an evidence of specificity of the agglutination reaction for the various strains of *Streptococcus hemolyticus* examined. Of the 50 control series, only 2 showed evidence of agglutinins for the strains of *Streptococcus hemolyticus* employed. Of 31 strains of other organisms used none was agglutinated by the sera of patients with rheumatoid arthritis to any significant titre. The present study supports the following hypothesis: Rheumatoid arthritis, in the majority of instances results from infection with *Streptococcus hemolyticus.* The evidence so far accumulated indicates that no specific strain of *Streptococcus hemolyticus* can be considered as the sole etiologic agent. No evidence has been found that the organisms gain access to the circulation or the joint tissues. The suggestion is advanced that the majority of cases of this disease represent the response of the affected tissues to products of *Streptococcus hemolyticus* absorbed from a distant focus.

Reviews

Modern Methods of Treatment. By LOGAN CLENDENING, M.D., Professor of Clinical Medicine, Lecturer on Therapeutics, Medical Department of the University of Kansas; Attending Physician, Kansas City General Hospital; Physician to St. Luke's Hospital, Kansah City, Missouri. With Chapters on Special Subjects by a Number of Writers. Fourth Edition. 819 pages, 95 fifigures, charts. C. V. Mosby Company, St. Louis, Mo. Price in cloth, $10.00.

The rapid sequence of editions of this book shows that it has met with a generous reception at the hands of practitioners, and this in turn means appreciation of its practical value. This edition has been carefully revised. The author has not endeavored to add every suggested change in therapy developed since the last edition; but the inclusions and additions are dependent upon the limitations of his experience and his judgment as to what methods are firmly established and supported by scientific evidence. The recent work on the chemistry of the thyroid principle, the use of desiccated swine stomach in pernicious anemia, salyrgan, postural rest in tuberculosis, Calmette's B.C.G. vaccination, undulant fever, ethylene, parathyroid hormone in Paget's disease, and hyperparathyroidism have all been described. The sections on myxedema, diabetic coma, diet in tuberculosis, cisterna puncture, and infantile paralysis have been rewritten. The general plan and purpose of the book have not been changed. It has apparently been found useful to practitioners of medicine. The author has had in mind the problems of the general practitioner, and has encouraged him to make use of methods that unfortunately are believed by many to belong to the so-called specialist. The original plan of his work was to furnish an outline of all the methods of treatment used in internal medicine, diet, drugs, hydrotherapy, blood transfusion, etc., all in one volume. In this book every department of medical therapeutics is covered; the first part of the book describes the procedure, the second part gives the indications for its application, based uopn the principles of physiological pathology. At the end of each chapter, the author has placed a short list of references in English, as more practical for those who may not have access to foreign works of reference. The author has succeeded admirably in his plan. His method of presentation has improved with the successive editions. He shows much practical good sense, as for example, his advocacy of the efficiency of spanking as opposed to psycho-analysis. This book will be very useful to the general practitioner in medicine.

How It Happened. By ADALBERT G. BETTMAN, M.D., F.A.C.P., 110 pages. F. A. Davis Company, Philadelphia, 1931. Price in cloth, $1.00.

This is a presentation of well-known facts in medicine through the medium of unrhymed poetic form, free verse. The poems, of which there are an even hundred, are given proper names for titles, and in many cases are presented in the names of both husband and wife, or of several members of the family. A large variety of medical subjects are treated, such as delay in diagnosis and treatment, incorrect diagnoses, rheumatic fever, appendicitis, tuberculosis, malaria, cancer, diphtheria, adenoids, patent medicines, the Dick test, horse asthma, mumps, and many others. Abortion and venereal diseases come in for as large a share of attention as they deserve. The solid facts are given; and this little book contains much that every layman should know. Each poem is a moral lesson in itself. How much these moral medical lessons gain by being presented in poetical form, it is of course, difficult to say, but they may make

an appeal to certain classes of our society. No one, however, can doubt the earnest motive behind their creation, and the medical facts here presented are sound beyond argument. There are many citizens throughout the country who can gain important knowledge from their perusal.

The Antiquity of Hindu Medicine and Civilization. By D. CHOWRY MUTHU, M.D., M.R.C.S., L.R.C.P., Lond.; Associate of King's College, London; Consulting Physician, Mendip Hills and Thumbaram Sanatoria. Third Edition. Enlarged. 112 pages. Paul B. Hoeber, Inc., New York, 1931. Price $1.50.

This little volume will serve the reader as an introduction to a brief survey of the antiquity of Hindu medicine and civilization. European scholars have been slow to admit the claims of the Hindus for the antiquity of their civilization. Recent archaeological discoveries in the Punjab and Sind have revealed the existence of a civilization of over five thousand years ago, showing a relatively high degree of luxury and social conditions much in advance of what was contemporary in Mesopotamia or Egypt. The discovery of some specimens of cinnabar in these ruins suggests that these ancient people knew how to extract mercury from this mineral, and indirectly proves the claim of the Hindus to their priority in making mercury. It is probably to the Hindus that we owe the first system of medicine; and the records of Hindu medicine may be traced as far back as the sixth century, B. C. The Hindu system of medicine forms a part of the Vedas, dating to at least 4000 B.C. Already in India, Vedic Medicine had so far advanced that the followers of the healing art were divided as surgeons, physicians, and magic doctors. The physicians lived in houses surrounded by gardens, containing medicinal plants which they collected and codified. The properties of a new drug were always praised in the Rig Veda, which gives the names of a thousand and one medicinal plants. The surgeons attended the ladies and acted as accoucheurs, giving medicine to relieve pain and suffering. There is an entire hymn of the Rig Veda devoted to the description and treatment of phthisis. In the Rig Vedic period, there were already signs of an advancement in surgery, midwifery, medicine, therapeutics, child management, and sanitation. In the latter Vedas the medical system takes on a more definite shape. Atharva Veda contains the oldest literary monument of Indian medicine. The Ayur Veda is the oldest systematic work on medicine, and formed the basis of the writings of subsequent medical authors for many centuries. Fragments of manuscripts exist, containing anatomical descriptions of various parts of the body. In the epic period there were two celebrated medical men, Charaka and Susruta, whose books were considered as standard works on Hindu medicine for many centuries, and were revised and re-edited as late as 1550 A.D. Charaka's book on medicine is voluminous, containing 120 chapters. It deals with diseases of the heart, chest, abdomen, genital organs, and lower extremities, their causes, symptoms, and treatment. Chapters are devoted to diet, drugs, antidotes, medical instruments, and appliances. Susruta was a great surgeon; and his work is mainly devoted to surgery. He describes 101 varieties of blunt instruments and 20 different kinds of sharp instruments. Most of the modern surgical instruments are but modifications of those used by the ancient Hindu surgeons. Susruta was the first to advocate dissection of dead bodies as indispensable for a successful surgeon. From the time of Buddha, surgery, anatomy, and dissection steadily declined, while chemistry and medicine increased in importance. Based upon relatively slight evidence, the author claims that the Hindus worked out the atomic theory, the evolution theory, the theory of motion, gravity, sound, light and heat, the presence of ether, the humoral theory, and the circulation of the blood, centuries before they became known to Europe. Much can be made out of very little and the modern Hindu has an exaggerated ego when it comes to recounting the achievements of his race. Nevertheless, this very egoism adds a touch of interest to this brief narrative of Hindu medicine, which would be lacking in the cold-blooded and condensed accounts given in the usual history of medicine. The book is of con-

venient pocket size, comparable to those of the Clio Medica series.

Clio Medica. Physiology. By JOHN F. FULTON, M.D., Sterling Professor of Physiology, Yale University. 141 pages, illustrated. Editor E. B. Krumbhaar, M.D. Paul B. Hoeber, Inc., New York, 1931. Price $1.50.

This is the fifth of the little volumes in red of the Clio Medica series. Physiology arose relatively late in the evolution of knowledge, since it depends ultimately upon analysis and reasoning, rather than upon observation and classification. Physiological knowledge derived from experiment began with Galen, who carried out vivisections on dogs, monkeys, and pigs, and studied the structure and functions of nearly every organ in the animal body. He discovered that aphonia followed cutting of the recurrent laryngeal nerve and that hemiplegia resulted from unilateral destruction of the brain. His experiments upon the physiology of the spinal cord rank as classics of physiologic literature. The first chapter is concerned particularly with Aristotle and Galen. In treating of the growth of physiology during the sixteenth and seventeenth centuries the author has found it desirable to follow three main themes: circulation, respiration, and digestion. Thus the unity of three of the most important subdivisions of physiology is preserved, and at the same time the chief personalities can be brought naturally into consideration. Chief attention has been given to the vascular system since all other branches of physiology were dependent upon the settlement of the problem of the circulation. After Aristotle and Galen, Chapter II deals with Harvey and the circulation of the blood; Chapter III is concerned with respiration, and Chapter IV with digestion. Chapter V treats of physiology in the nineteenth century and the use of the teaching laboratories. There is an epilogue "The Trend of Modern Physiology," an appendix "La Physiologie Générale," a short bibliography, and name and subject indices. The growth of neurology and neurophysiology is given but scant mention; as are also biochemistry and biophysics. The author has dealt with the evolution of the main facts of what is generally termed physiology in the older conception of the term, as expressed by circulation, respiration, and digestion. He has followed the more personal manner of treatment of the subject, believing correctly, that personal details of the lives of the chief actors in the history of physiology make a more appealing tale, and engage more closely the interest of the medical student for whom the book is primarily intended. The author has succeeded in presenting this history in an interesting and readable manner, largely because of the frequently exercised human touch. It is a very good performance, and he may be congratulated upon it.

Arterial Hypertension. By EDWARD J. STIEGLITZ, M.S., M.D., Assistant Professor of Clinical Medicine, Rush Medical College, University of Chicago. Attending Internist, Chicago Lying-in Hospital, Assistant Attending Physician, Presbyterian Hospital. Foreword by Rollin T. Woodyatt, M.D., Clinical Professor of Medicine, Rush Medical College, University of Chicago; Chairman Department of Medicine; Attending Internist, Presbyterian Hospital. 280 pages, 21 illustrations. Paul B. Hoeber, Inc., New York, 1930. Price $5.50.

The present monograph is based upon a series of lectures given at Rush Medical College during the last several years. It represents an attempt to discuss the problems of cardiovascular-renal disease and hypertension in such a manner that the logic of physiologic mechanism may be used at the bedside. The menace of arterial disease with hypertension and the subsequent threat of cardiac failure is apparently increasing; at least, the clinical occurrence of such cases has increased, and in clinical practical work the frequency and importance of arterial disease are constantly being emphasized. Because of their chronicity and asymptomatic nature the significance of the processes of arterial disease have been given inadequate attention in the past. The author lays emphasis upon the etiologic processes of arterial hypertension and upon the physiologic pathogenesis; he interprets all therapeutic procedures in view of their physiologic applications; emphasizing the reasons

and mechanism underlying the processes involved. He prefers the term arterial hypertension to that of high blood pressure, since the latter calls attention to the blood rather than to the vascular structures themselves. Hypertension per se represents a physiologic reaction occurring in disease of the smaller arterioles, and is in itself not a disease. Arteriolar hypertonia is the fundamental change; the increase in intravascular pressure is secondary thereto. The subject matter is treated in nine chapters: The Problem; Anatomy, Physiology, and Pathogenesis of Hypertension; Symptoms of Hypertension; Treatment; Prognosis; Factor of Cardiac Reserve; Factor of Renal Reserve; and Arterial Hypertension in Pregnancy. There is a fairly complete bibliography, and a bibliographic subject index. The chapter on etiology is an excellent survey of the problem, and the author's conclusions are notable for their analytical sanity. Similarly well done is the chapter on Symptoms; that on treatment shows the same high degree of sound sense. Altogether this book constitutes an excxellent survey of the subject; and can be recommended to practitioners as necessary to their libraries. It is the most practical and complete resumé of the subject of which the reviewer has knowledge.

The Right Honourable Sir Thomas Clifford Allbutt, K.C.B.A. Memoir. By Sir Humphrey Davy Rolleston, Bart., G.C.V.O., K.C.B., M.A., M.D., D.Sc., LL.D.; Regius Professor of Physic in the University of Cambridge; Sometime President of the Royal College of Physicians of London. 314 pages. MacMillan and Co., Ltd., London, 1929.

This life of Sir Clifford Allbutt was written at the request of Lady Allbutt. From the beginning the author was handicapped by the paucity of personal material. In spite of his manifold activities extending over wide fields and many years, full materials for an adequate and accurate account have not been at hand. He kept very few letters, did not write a diary, or leave any unpublished reminiscences and very few of his early contemporaries are now alive. The resultant biography is, therefore, not much more than a chronological record, derived chiefly from published sources, such as medical and other journals, and from textbooks. Although this record indicates the wonderful energy, versatility, wide sympathies and scholarly culture of this leader of his profession, the work certainly lacks the interest of the human touch. It is bibliographical, rather than biographical. Yet, Sir Humphrey Rolleston has contrived out of relatively meager data to present a readable and interesting picture of Allbutt, and to permit of a sympathetic evalution of his life.

College News Notes

Dr. Hugh S. Cumming (Fellow), Surgeon General of the U. S. Public Health Association, is the President of the American Public Health Association for the present year.

Dr. Henry Mason Smith (Fellow), Tampa,, is President of the Florida State Board of Health.

Dr. Felix J. Underwood (Fellow), Jackson, Miss., is President of the Southern Medical Association for the present year.

One of the endowed hospitals to serve as centers for the treatment of diabetes, as proposed by Dr. Elliott P. Joslin (Fellow), Harvard University Medical School, will be erected in St. Louis.

In connection with the forty-seventh annual convention of the Tri-State Medical Association of Mississippi, Arkansas and Tennessee, held at Memphis, February 17-20, the following members of the College were on the program:

Dr. F. T. Lord (Fellow), Boston, Mass.

Dr. Alfred Scott Warthin (Master), Ann Arbor, Mich.

Dr. William Gerry Morgan (Fellow), Washington, D. C.

Dr. C. C. Sturgis (Fellow), Ann Arbor, Mich.

Col. Charles F. Craig (Fellow), Washington, D. C.

Dr. G. W. McCoy (Fellow), Washington, D. C.

Dr. A. C. Ivy (Fellow), Chicago, Ill.

Dr. A. F. Cooper (Fellow), Memphis, is the Secretary-Treasurer of this Association.

Dr. Henry H. Turner (Fellow), Oklahoma City, has returned after spending three months in postgraduate study of neurology in London and Vienna.

Dr. T. F. Abercrombie (Fellow), Atlanta, addressed the Georgia Public Health Association, January 16-17, on "Proposed Public Health Legislation, State and National."

Dr. Clyde Brooks (Fellow), formerly Dean of the School of Medicine, University of Alabama, has accepted the post as Professor of Physiology and Pharmacology in the School of Medicine which is now being organized in New Orleans under the auspices of Louisiana State University. The new school will begin its first session next fall with a class of Freshmen and a class of Junior medical students. A new building for the school is now going up on the campus of Charity Hospital, New Orleans.

In the February, 1931, Issue of THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, the following Fellows of the College are authors of articles indicated:

Dr. H. M. Winans, Dallas, Texas: "Leukemoid Blood Picture in Pseudomucinous Cyst and Papillary Adenoma of the Ovary";

Dr. Thomas Fitz-Hugh, Jr., Philadelphia, Pa.: "Splenomegaly and Hepatic Enlargement in Hereditary Hemorrhagic Telangiectasia."

Dr. J. Allison Hodges (Fellow), President of the Medical Society of Virginia, delivered an address on "The Medical Practitioner's Interest in Public Health" at the annual meeting of the State Public Health Nurses at Richmond, January 6.

Dr. Hodges, with other members of the Committee on Tuberculosis Clinics of the Medical Society of Virginia, including Dr. C. Lydon Harrell (Fellow), Norfolk, held a conference with officials of the State Board of Health at Richmond on January 19, for the discussion of tuberculosis clinics and the work of the X-ray service of the Department of Health.

Dr. Henry A. Christian (Fellow), Boston, was the speaker at a dinner, February 16, in connection with the Annual Congress of Medical Education, Medical Licensure and Hospitals held in Chcago.

Dr. Beverley R. Tucker (Fellow), Richmond, was Chairman of the Committee on Arrangements for the 33d annual meeting of the Tri-State Medical Association of the Carolinas and Virginia held at Richmond, February 16-17.

Dr. Louis Hamman (Fellow), Baltimore, was one of the invited guests who delivered an address and gave a clinic.

Dr. Lea A. Riley (Fellow), Oklahoma City, was recently reappointed the member of the Council from Oklahoma of the Southern Medical Association by its President, Dr. Felix J. Underwood (Fellow), Jackson, Miss.

Dr. John A. Lanford (Fellow) and Dr. Daniel N. Silverman (Fellow), both of New Orleans, were elected Treasurer and Librarian, respectively, of the Orleans Parish Medical Society at its last annual meeting.

Dr. Lewellys F. Barker (Fellow), Baltimore, was the banquet speaker at the Southeastern Surgical Congress held at Atlanta, March 9-10. Dr. Barker's subject was "The Necessity for Close Relationship Between the Modern Internist and the Up-to-date Surgeon."

Dr. William R. Bathrust (Fellow), Little Rock, was elected Treasurer of the Pulaski County (Ark.) Medical Society at its last annual meeting.

Dr. David Riesman (Fellow), Professor of Clinical Medicine at the University of Pennsylvania School of Medicine, has been appointed Consultant to the Committee on the Costs of Medical Care.

Dr. Frank Smithies (Master), Chicago, has been elected a foreign member of La So Société Médicale des Hōpitaux de Paris.

Dr. Harold S. Hulbert (Fellow), Chicago, discussed the subject of physically and mentally handicapped children at a statewide conference on child health and protection held in Indianapolis, January 15-17.

At the annual dinner meeting of the Marlboro County (S. C.) Medical Society held January 9 at the Marlboro County General Hospital at Bennettsville, the following delivered addresses:

Dr. Stewart R. Roberts (Fellow), Atlanta, Ga.:
"Thyroid Heart"

Dr. Edgar A. Hines (Fellow), Seneca, S. C.:
"Progress in Medical Economics"

Dr. James B. Sidbury (Fellow), Wilmington, N. C.:
"Viosterol and Cod Liver Oil in the Treatment of Rickets"

Dr. Robert Wilson (Fellow), Charleston, S. C.:
Clinic on medical cases.

Dr. Kenneth M. Lynch (Fellow), Charleston, S. C.:
"Public Medicine Versus Private Practice

Dr. Carl V. Weller (Fellow), delivered an address on "Primary Carcinoma of the Lung," before the Academy of Medicine, of Cincinnati, on February 2, 1931.

Dr. Anton J. Carlson (Fellow), of the University of Chicago, addressed the final session, Section I, Committee A, of the White House Conference on Child Health and Protection on physiologic considerations at Washington, February 19-21.

Dr. George R. Minot (Fellow), Professor of Medicine at the Harvard University Medical School, and Dr. William P. Murphy, Instructor in Medicine at the same institution, received the 1930 Cameron Prize of the Faculty of Medicine of Edinburgh University in recognition of their work on the treatment of pernicious anemia.

Dr. Henry A. Christian (Fellow), Boston, addressed the Harvard Medical Society, January 13, on "Clinical Classification of Nephritis".

Dr. Charles L. Brown (Fellow), Ann Arbor, addressed the Oakland County Medical Society at Pontiac, Michigan, January 16, on "Clinical Use of Diuretics".

Dr. David Marine (Fellow), Director of Laboratories of the Montefiore Hospital and Assistant Professor of Pathology at the College of Physicians and Surgeons of Columbia University, was the recipient of a gold medal presented by the New York Academy of Medicine, January 7, in recognition of his research into the structure, functions and diseases of the thyroid gland.

Dr. William Gerry Morgan (Fellow), Washington, D. C., spoke before the Lycoming County (Pa.) Medical Society at Williamport, January 9, on "Observations on Etiology".

Dr. Lewellys F. Barker (Fellow), Baltimore, discussed the interrelated functions of the dentist and family physician in preventive fields, January 5, before the joint meeting of the Cleveland Dental Society and the Cleveland Academy of Medicine.

Dr. Howard T. Karsner (Fellow), Professor of Pathologist at the Western Reserve University School of Medicine, Cleveland, has been elected Chairman of the section on medical sciences of the American Association for the advancement of Science.

Dr. Karsner was one of the speakers on a symposium on medicine and law conducted before the joint meeting of the Cleveland Academy of Medicine and the Cleveland Bar Association on January 6.

"Multiple Cares, Costs, Trends and Problems of Today" was the subject of an address given, January 15, by Dr. Stewart R. Roberts (Fellow), Atlanta, before the Fulton County (Ga.) Medical Society.

Dr. Lester R. Dragsteda (Fellow), Chicago, addressed the Chicago Society of Internal Medicine, January 26; his subject being, "Significance of Failure of Reabsorption of Digestive Juices in Some Gastro-Intestinal Disorders".

Dr. George E. Pfahler (Fellow), Philadelphia, addressed the Philadelphia Urological Society, January 26, on "Diagnosis and Treatment of Bladder Tumors from the Roentgenolofic Standpoint".

On January 1, Dr. W. S. Leathers (Fellow), Dean and Professor of Preventive Medicine and Public Health at Vanderbilt University School of Medicine, was appointed a member for a term of five years of the National Advisory Health Council of the U. S. Public Health Service.

Dr. Hugh S. Cumming (Fellow), Surgeon General of the U. S. Public Health Service, presided at a symposium on cancer research held under the auspices of the National Institute of Health, January 7.

Dr. LeRoy S. Peters (Fellow), Albuquerque, N. M., delivered a paper entitled, "Cauterization of Adhesions in Artificial Pneumothorax" before the Jackson County (Kans.) Medical Society, February 3.

Dr. Sidney K. Simon (Fellow), New Orleans, has been elected President of the American Society of Tropical Medicine.

Dr. A. G. Sullivan (Fellow), Hot Springs, addressed the Pulaski County Medical As-

sociation of Little Rock, February 2, on "Acute Occlusion".

Doctors L. C. Towne (Fellow), Milton Shaw (Fellow), L. G. Christian (Fellow) and T. I. Bauer (Associate), all of Lansing, Mich., held a symposium on Heart Disease before the Livingston County Medical Association at Howell, February 10.

Dr. B. P. Stivelman (Fellow), New York City, has recently been promoted to the position of Attending Physician to the Harlem Hospital, and Associate Physician to the Riverside and Jewish Memorial Hospitals, New York City.

Dr. Joseph G. Terrence (Associate), Brooklyn, was promoted, during November, 1930, to Attending Physician to Kings County Hospital.

Dr. L. T. LeWald (Fellow), Professor of Ronetgenology, New York University, read a paper entitled "Roentgen Evidence of Osseous Manifestations of Certain Types of Anemia, with Special Reference to Mediterranean Anemia" at the annual meeting of the Radiological Society of North America at Los Angeles, December 5, 1930.

Dr. George Howard Spivey (Fellow), formerly of Gainesville, Texas, has recently become the Director of the Maricopa County Health Unit of Phoenix, Arizona.

Dr. C. C. Wholey (Fellow), Pittsburgh, is Chairman of the Allegheny County Division of the Mental Hygiene Commission of the Medical Society of the State of Pennsylvania.

Dr. Wholey is the author of an article entitled "The Super-Normal and the Emotionally Unstable Child" in the December Issue of the Pittsburgh School Bulletin.

In this same journal and the same issue, Dr. E. Bosworth McCready (Fellow), Pittsburgh, is the author of an article entitled, "The Duty of the School to the Child Requiring Special Attention".

Dr. A. J. Bruecken (Fellow), Pittsburgh, addressed the Pittsburgh Urological Association, December 11, on "Clinical Significance of Reactions".

Dr. Oliver T. Osborne (Fellow), New Haven, Conn., is the author of an article entitled "Medical Examinations for Life Insurance" in the Medical Journal and Record, December 3, 1930.

Dr. David Riesman (Follow), Philadelphia, recently delivered an address on "The Care of the Patient or the Art of Medicine" at the Harvard Medical School. He also spoke before the Academy of Medicine of Columbus, Ohio, on "High Blood Pressure".

Dr. Herman B. Allyn (Fellow), Philadelphia, has been re-elected Chairman of the Section on the History of Medicine of the Philadelphia College of Physicians. He read a paper on "Oliver Wendell Holmes; His Wisdom and Humor" at the December meeting of the Section.

In the December Issue of the American Journal of The Medical Sciences, the following Fellows are authors of articles indicated:

Dr. David Marine, New York, N. Y.:
"Remarks on the Pathogenesis of Disease"

Dr. Lewis M. Hurxthal, Boston, Miss:
"The Size of the Heart in Goiter. A Teleroentgenographic Study" (with Dr. O. J. Menard and Dr. M. E. Bogan)

Dr. L. N. Boston, Philadelphia, Pa.:
"Gastric Hemorrhage Due to Familial Telangiectasis"

Dr. Benjamin Goldberg, Chicago, Ill.:
"Epituberculosis. A study of Ten Cases for a Period of Over Two Years" (with Dr. Benjamin M. Gasul)

Dr. William Gerry Morgan (Fellow), Washington, D. C., addressed the Los An-

geles County Medical Association, December 5.

Dr. O. H. Perry Pepper (Fellow), Philadelphia, gave the annual Scripps Metabolic Clinic Lectures in San Diego, Calif., January 8-10.

Dr. Samuel M. Feinberg (Fellow), Chicago, addressed the first meeting of the Chicago Society of Allergy, December 22, on "Historical Aspects of Allergy".

Dr. William A. Evans (Follow), Detroit, addressed the Chicago Roentgen Society, December 10, on "Indications for the Results of Surgical Treatment of Pulmonary Lesions as Observed Roentgenologically".

Dr. Benjamin Goldberg (Follow), also of Chicago, spoke before the same meeting on "Roentgenologic Aspects of Pulmonary Tuberculosis in Childhood".

Dr. Joseph L. Miller (Fellow), Chicago, addressed the Chicago Society of Internal Medicine, December 15, on "Classification, Etiology and Pathology of Chronic Arthritis".

Dr. George R. Minot (Fellow), Boston, gave the seventh of a series of afternoon lectures at the New York Academy of Medicine, January 9; his subject being "Treatment of Anemia".

Dr. Joseph C. Doane (Fellow), Philadelphia, was elected the President of the American Occupational Therapy Association at New Orleans during the latter part of October.

The Medical Society of the City and County of Denver was addressed, December 2, by Dr. William B. Yegge (Fellow), Denver, on "Polycythemia", and by Dr. Philip Work (Fellow), Denver, on "Multiple Fat Emboli".

Dr. George H. Coleman (Fellow), Chicago, and Dr. John Favill (Fellow), Chicago, were elected Secretary and Treasurer, respectively, of the Institute of Medicine of Chicago on December 3.

Dr. Oscar B. Hunter (Fellow), Chicago, spoke before the Medical and Chirurgical Faculty of Maryland, December 5, on "Progressive Gangrene of the Abdominal Wall".

The Greater Boston Medical Society was addressed, December 2, by Dr. Solomon Strouse (Fellow), Chicago, on "Medical Complications of Pregnancy".

Dr. Elliott P. Joslin (Fellow), Boston, delivered the third of a series of monthly lectures before the William Harvey Sosociety of Tufts Medical School, Boston, December 12, on "The Carbohydrates in the Body".

Dr. Torald H. Sollman (Fellow), Professor of Pharmacology and Materia Medica, and Dean of the Medical School of Western Reserve University, delivered the fifteenth Mellon Lecture, December 5, on "Clinical Excretion of Mercury", the lecture being sponsored by the Biological Society for Research of the University of Pittsburgh.

Dr. Wilbut C. Davison (Fellow), Durham, N. C., and Dr. Walter A. Baetjer (Fellow), Baltimore, Md., addressed the thirty-fifth annual session of the Seaboard Medical Association of Virginia and North Carolina at Elizabeth City, N. C., December 2-4, on "The Duke Medical School" and "Infectious Arthritis", respectively.

Dr. James M. Anders (Master), Philadelphia, gave "A Historic Sketch of the Philadelphia County Medical Society" at the Anniversary Dinner to commemorate the eighty-second birthday of the Philadelphia County Medical Society, January 14. Dr. Anders also gave a Health Radio Talk, December 30, entitled "Why the Laity Fails to Preserve a High Standard of Health", under the auspices of the Philadelphia County Medical Society.

Dr. Carl V. Vischer (Fellow), Philadelphia, is co-author with Dr. E. O. Geckeler of "A Clinical Investigation of Chronic Arthritis, with Special Reference to Treatment", which was published in the January number of the Hanhemannian Monthly. This is a detailed report of the research work done by Doctors Vischer and Geckeler on Chronic Arthritis during the past two years. The investigations were carried out in the Arthritis Conference of the Hahnemann Hospital of Philadelphia.

Dr. Edward E. Cornwall (Fellow), Brooklyn, addressed the Southside Medical Society at Babylon, December 17, on "The Treatment of Pneumonia".

Dr. Carl R. Howson (Fellow), Los Angeles, was elected President of the Los Angeles County Medical Association at the annual meeting held on December 18.

Dr. Leon T. LeWald (Fellow), New York, was elected President of the New York Gastro-enterological Association for the year 1931.

Dr. Donald R. Ferguson (Fellow), Philadelphia, is the author of an article entitled "Some Problems in Diabetes", which appeared in the December number of the Hahnemannian Monthly. The original paper was read before the Homeopathic Medical Society of the State of Pennsylvania in September.

Dr. George G. Hunter (Fellow), Los Angeles, was elected President of the Los Angeles Clinical and Pathological Society for the year 1931.

Dr. E. J. G. Beardsley (Fellow), Philadelphia, addressed the Sussex County Medical Society at Georgetown, Delaware, on "Common Cardio-vascular Disorders of General Practice", December 12.

Dr. David Riesman (Fellow), Philadelphia, was the speaker at a Postgraduate Seminar of the Philadelphia County Medical Society on January 9, his subject being "The Failing Heart of Middle Life". Dr. E. J. G. Beardsley (Fellow), Philadelphia, introduced the speaker.

Dr. Frank Smithies (Master), Chicago, was elected First Vice President of the American Society of Tropical Medicine on December 30.

Dr. H. Brooks Mills (Fellow), Philadelphia, was recently elected Consulting Pediatrist to the Northwestern General Hospital.

Dr. Mills also recently addressed the Optimist Club of Doylestown, Pa., on "The Child of Today—The Adult of Tomorrow".

Dr. Linn J. Boyd (Fellow), New York, is the author of an article entitled, "The Constitutional Factor in Disease", which appeared in the January Issue of the Journal of the American Institute of Homeopathy.

The following Fellows of the College are authors of articles indicated, which appeared in the January, 1931, Issue of THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES:

Dr. George R. Minot, Boston, with Stacy R. Mettier, M.D.: "The Effect of Iron on Blood Formation as Influenced by Changing the Acidity of the Gastro-duodenal Contents in Certain Cases of Anemia".

Dr. Leonard F. C. Wendt, Detroit, with Franklin B. Peck, M.D.: "Diabetes Mellitus. A Review of 1073, 1919-1929.".

Dr. Moses Paulson, Baltimore, with Justin Andrews, Sc.D.: "The Incidence of Human Intestinal Protozoa, with Especial Reference to Endamoeba Histolytica, in the Residents of the Temperate Zone".

Dr. George Morris Piersol (Fellow and Secretary-General of the College), Philadelphia, is the author of an article entitled, "Acute Indigestion", which appeared in the January 3 number of the Weekly Roster and Medical Digest.

Dr. John B. Hawes, 2nd (Fellow), Boston, is the author of a new book entitled "Talks on Tuberculosis: With Patients and Their Frineds", being published by the Houghton Mifflin Company.

Dr. Hawes has been President of the Boston Tuberculosis Association for the past ten years; he is Consultant, Diseases of the Chest, to the Beth Israel Hospital and is a Director of the Massachusetts Tuberculosis League and the National Tuberculosis Association.

Dr. C. B. Burr (Fellow), Flint, was the Chairman of the Committee of the Michigan State Medical Society which has prepared, in two volumes, "Michigan's Medical History". Dr. Burr personally contributed chapter on the following subjects: the Physician mainly from the Layman's Viewpoint, the American Indian, his Medicine, etc., Physicians with the Early Explorers and Adventurers, Eighteenth Century Physicians, Pioneer and Early Physicians, Therapy Then and Now, Women Physicians, Medical Societies, Extra-professional Activities.

The University of Michigan, in accordance with its newly inaugurated plan of granting an honorary degree, M.A., to some physician of outstanding ability or accomplishment in that city, at the fall Convocation of students of the medical school, choose Dr. Burr for the first such degree to be conferred.

Dr. Edgar F. Kiser (Fellow), Indianapolis, with Dr. C. B. Bohner, addressed the Indianapolis Medical Society, January 27, on "Incidence of Syphilis in Private Practice; an Analytical Study of 2329 Cases, Based on Serological Tests".

D. Ellis M. Frost (Fellow), Pittsburgh, addressed the Allegheny County Medical Society, January 20, on "Differential Diagnosis of Emypema".

Dr. C. L. Palmer (Fellow), Pittsburgh, was chairman of the Program Committee.

Dr. W. Stanley Curtis (Fellow), Boston, is in charge of the Medical Department of the Youngstown Clinic, which was opened last October. Dr. Curtis was formerly an Associate of Dr. Elliott P. Joslin (Fellow), Boston.

Dr. Walter C. Alvares (Fellow), Rochester, Minn., will address the Dallas Southern Clinical Society at their Third Spring Clinical Conference, March 30-April 3.

Dr. Ada E. Schweitzer (Fellow), Indianapolis, was the Chairman of the Program Committee for the Indiana Conference on Child Health and Protection at Indianapolis, January 15-17.

Dr. H. S. Hatch (Fellow), formerly of Indianapolis, has recently moved to Morristown, N. J., to take charge of the Tuberculosis work in that County.

Dr. H. O. Colomb (Associate), formerly of St. Elizabeth's Hospital, Washington, D. C., is now Director of the Psychopathic Department of the Providence City Hospital, Providence, R. I.

Dr. LeGrand Kerr (Fellow), Brooklyn, was elected President of the Medical Association of the Greater City of New York, January 19. This Society comprises all of the five boroughs of the City, and meetings are held monthly at the Academy of Medicine in Manhattan, with the exception that one meeting a year is held in each of the four other boroughs.

Dr. Kerr's presidential address was delivered on February 16, his subject having been "The Physician and his Literature".

Dr. J. L. McCartney (Fellow), Chief of the Division of Mental Hygiene, Connecticut State Department of Health, has drawn up a chart of averages of "normal" child development. This chart is being distributed to parents as an experiment in positive mental hygiene. The chart covers the essential points from birth to twenty-one years of age, the five angles of de-

velopment: physical, senses and emotion, habits, education, sociability and play.

Dr. O. R. Witter (Fellow), of Hartford, Conn., was elected President of the Hartford Medical Society, at the annual meeting, Jan. 5, 1931. Dr. C. Brewster (Fellow), was elected Vice-President. The address of the evening was giving by the retiring president, Dr. Edward J. Turbert (Fellow), who spoke in "Subsidies by the State for the Care of Dependent Sick".

Dr. R. A. C. Wollenberg (Fellow), Detroit, addressed the St. Clair County Medical Society on the subject of "Skin Cancer and its Prophylaxis", December 16, at Port Huron, Michigan.

Dr. William J. Stapleton, Jr. (Fellow), Detroit, gave an illustrated talk before the Saginaw Valley Medical Society, January 20, on "Hospitals and Clinics in Europe".

Dr. William Egbert Robertson (Fellow), Philadelphia, Professor of Medicine at Temple University, gave a Health Radio Talk, "The Heart, a Master Pump", on January 20, under the auspices of the Philadelphia County Medical Society.

Dr. Irving Gray (Fellow), Brooklyn, addressed the Richmond County Medical Society of Staten Island, February 11, on "Recent Advances in Gastro-Intestinal Diseases".

Dr. Oliver T. Osborne (Fellow), New Haven, Conn., is the author of an article entitled, "Medical Mentor", which appeared in the MEDICAL MENTOR, January, 1931, pages 6, 7 and 8, Volume II, No. 1.

Dr. Logan Clendening (Fellow), Kansas City, Mo., has tendered his resignation as a Regent of the American College of Physicians, as of December 15.

Dr. Charles G. Jennings (Master) and Dr. A. F. Jennings (Fellow) have announced the removal of their offices to the Charles Godwin Jennings Hospital, 7815 Jefferson Avenue, East, Detroit, Michigan.

Dr. Fred W. Wilkerson (Fellow), Montgomery, Ala., was the author of an article on "Sprue Tested with Liver" in the October, 1930, Issue of the Southern Medical Journal.

NEW LIFE MEMBERS

The following members of the American College of Physicians have subscribed to the Endowment Fund and have become Life Members on the dates indicated:

Sydney R. Miller (Fellow), Baltimore, Md., January 22, 1931

William H. Gordon (Fellow), Detroit, Mich., January 22, 1931

Samuel Weiss (Fellow), New York, N. Y., February 4, 1931

James M. Anders (Master), Philadelphia, Pa., February 7, 1931

The attention of Fellows and Masters everywhere is particularly called to a pamphlet entitled "The Creation of an Endownment Fund for the American College of Physicians", published and distributed by the President of the College and the Chairman of its Finance Committee during January of the present year. This pamphlet discloses the objects and needs of the College for an Endowment Fund, and points out the advantages to members by subscribing to Life Membership. All monies received for Life Memberships in the College, including the original initiation fee of such members, are transferred immediately to the Endowment Fund of the College,, the principal of which is held intact and invested in securities approved by the Board of Regents, while the income only is available for carrying out the purposes of the organization.

GIFTS TO THE COLLEGE LIBRARY

Acknowledgment is herewith made of the receipt of the following donations of reprints and books to the College Library of publications by members:

Dr. Oscar W. Bethea (Fellow), New Orleans, La.:

4 Reprints:
"The Treatment of Hyperchlorhydria"
"A Treatment of Pneumonia"
"Dangers in the Use of Barbituric Salts"
"Some Suggestions in Physical Diagnosis"

Dr. Grafton Tyler Brown (Fellow), Washington, D. C.:
1 Reprint:
"Linseed Meal Sensitization"

Dr. Warren Coleman (Fellow), New York, N. Y.:
1 Reprint:,
"Studies on the Flora of the Intestinal Tract"
(With Annis E. Thomson, M.D. & Max Einhorn, M.D., F.A.C.P.)

Dr. Alexander T. Cooper (Fellow), Denver, Colo.:
1 Reprint:
"Phrenicoexeresis in Pulmonary Tuberculosis"

Dr. Edward E. Cornwall (Fellow), Brooklyn, N. Y.:
45 Reprints:
"Physiologically Supportive Treatment of Pneumonia"
"The Management of the Heart in Pneumonia"
"Management of the Alimentary Tract in Pneumonia"
"Some Don'ts in the Treatment of Pneumonia"
"The Conservative Treatment of Pneumonia"
"On the Use of Digitalis in Pneumonia"
"What is Strophanthin? A Pharmacological & Pharmacodynamical Survey"
"The Dosage and Administration of Strophanthin"
"Milk as a Food for Human Adults"
"On Eating to the Best Advantage"
"Coffee in Health and Disease"
"A Plan of Feeding in Typhoid Fever"
"The Limitations of Digitalis"
"Septic Endocarditis Involving the Right Heart"
"Extrasystoles"
"Concerning Endocardial Murmurs"
"A Plan of Rectal Feeding"
"A Diabetic Dietary"
"When and How to use Nitrogylcerin"
"Paroxysmal Tachycardia"
"Intestinal Putrefaction Toxemias"
"Arthritis Deformans and its Relation to Intestinal Putrefaction"
"Clinical Significance of Variations in the Systolic and Diastolic Blood-Pressures and the Pulse-Pressure"
"Pick's Syndrome, with Report of a Case"
"Chronic Tobacco Poisoning and the Circulation"
"Clinical Study of a Case of Chronic Intestinal Toxemia of Severe Type"
"Some Conservative Aspects of Constipation Therapy"
"The Commonest Focal Infection"
"Clinical Study of a Case of Epilepsy Apparently of Intestinal Origin"
"Functional Disorder of the Circulatory Apparatus"
"The Direct Treatment of Heart Failure"
"Remarks on Constipation"
"Medical Notes on Early New England"
"The Prescribing of Diabetic Diets"
"On Living Longer"
"Some Practical Points in the Treatment of Obesity"
"The Remarkable Case of Luigi Cornaro and how he Balanced his Diet"
"A Simple Treatment for Restlessness and Insomnia"
"Alcohol in Medicine"
"The Fundamental Therapeutic Principle"
"Remarks on the Cardiac Arrhythmias and their Identification by Methods Which Are Generally Available"
"A Point in Stomatology"
"Medical Treatment of Gastric Ulcer"
"A Perfect Meal"
"Treatment of Fecal Impaction"

Dr. Donald R. Ferguson (Fellow), Philadelphia, Pa.:
2 Reprints:
"The Clinical Course of Primary Carcinoma of the Bronchi and Lung"
"Clinical Aspects of Massive Collapse of the Lung"

Dr. John H. Foster (Fellow), Waterbury, Conn.:
2 Reprints:
"Observations on Trichinosis"
"The Practice of Medicine in China and New England with Observations on Hypertension"

Dr. Hyman I. Goldstein (Associate), Camden, N. J.:
20 Reprints:
"Argyria from Argyrol"
"Cancer of the Liver and the Gall Bladder"
"Discussion on Blood Pressure"
"Family Obesity; Obesity in Children"
"Gastro-Intestinal Sarcoma"
"Gonococcemia and Metastatic Gonorrhea"
"Heart Irregularities and the Electrocardiograph"
"Meralgia Paresthetica (Roth's or Bernhardt's Disease)"
"Mono-Osteitic Paget's Disease of the Bones" (with Henry Zuckerman Goldstein, M.D.)
"Newer Therapy of Cardio-vascular Renal Disease" (with Leopold Goldstein, M.D., and Henry Z. Goldstein, M.D.)
"Notes on Meningitis"
"Paget's Disease of the Bones (Osteitis Deformans)"
"Pneumococcus Meningitis Case Reports with and without Pneumonia" (with Abelardo Gonzales, M.D.)
"Primary Malignant Tumors of the Liver"
"Primary Nodular Cancer of the Pancreas"
"Primary Sarcoma of the Appendix"
"Recent Advances in Treatment; Angioxyl in Angina Pectoris, and Hypertensive Conditions"
"Serum Disease"
"Sore Throat and Diphtheria"
"Sporadic Cretinism"
"Weil's Disease or Icterus Gravis (Acute Infectious Jaundice)

Dr. Ralph O. Clark (Fellow), New York, N. Y.:
1 Reprint:
"Vaccines: Their Use in the Control and Cure of Disease"

Dr. Joseph R. Darnall (Associate), Washington, D. C.:
5 Reprints:
"A Case of Chloroma of the Sacrum"
"Modern Conception and Rational Treatment of Diabetes Mellitus"
"Dietetic Management of Cardiac, Vascular and Renal Diseases" (2 copies)
"The Application of Occupational Therapy to Chronic Medical Cases" (2 copies)
"Diet in Heart and Kidney Disease"

Dr. W. Forest Dutton (Associate), Amarillo, Texas:
4 Reprints:
"Parenteral Medication"
"A Clearing House for Trite Papers"
"The Future of Medicine"
"Progress in Chemotherapy"

Dr. Samuel M. Feinberg (Fellow), Chicago, Ill.:
11 Reprints:
"Household Objects as Causes of Hypersensitiveness"
"The Nonspecific Diagnosis of Allergic Disease: Further Observations"
"Clinic of Dr. Samuel M. Feinberg—"Asthma Due to House Dust"
"Hay-Fever Treatment"
"Progress in Hay Fever"
"Seasonal Hay Fever Not Due to Pollen"
"The Vital Capacity in Bronchial Asthma"
"The Nonspecific Diagnosis of Allergic Asthma"
"Nasal Allergy as Related to Hay Fever and Hyperesthetic Rhinitis"
"The Management of the Asthmatic"
"The Relation of Asthma to Broncho-Pulmonary Infections and Inflammations"

Dr. Murray B. Gordon (Fellow), Brooklyn, N. Y.:
6 Reprints:
"The Effect of External Temperatures on the Sedimentation Rate of the Red Blood Corpuscles"

"Morphological Changes in the Endocrine Glands in Mongolian Idiocy with Report of Two Cases"
"An Endocrine Consideration of von Recklinghausen's Disease: Report of a Case with Associated Childhood Myxedema"
"Cholesterol and Lipoid Phosphorous in Infancy and in Childhood"
"The More Embrace Reflex in Infancy"
"Differential Diagnosis Between Diphtheria and Oral Lesions of Blood Dyscrasias" (with Dr. Abraham M. Litvak)

Dr. John W. Meehan (Fellow), Washington, D. C.:
1 Reprint:
"The Army Medical Center"

Dr. Oliver T. Osborne (Fellow), New Haven, Conn.:
1 Reprint:
"Medical Examinations for Life Insurance"

Dr. Edward O. Otis (Fellow), Exeter, N. H.:
1 Reprint:
"The Prevention of Disease"

Dr. William D. Reid (Fellow), Boston, Mass.:
1 Reprint:
"Pregnancy and Heart Disease"

Dr. J., W. Torbett (Fellow), Marlin Texas:
1 Reprint:
"Classification, Diagnosis and Treatment of Arthritis"

Dr. Edgar F. Kiser (Fellow), Indianapolis, Ind.:
1 Reprint:
"Ceremonial Circumcision"

Dr. L. J. Moorman (Fellow), Oaklahoma City, Okla.:
8 Reprints:
"Evil Results of Indiscriminate Removal of Tonsils in Adults"
"Tuberculosis in Medical Curricula"
"Teaching Medical Students the Normal Body"
"Recent Progress in the Treatment of Pulmonary Tuberculosis"
"The Relation of Advanced Pulmonary Tuberculosis to Manifest Tuberculosis in Infancy and Early Childhood"
"Our Debt to Aristotle"
"Massive Collapse (Atelectasis) of the Lung, with a Case Report"
"Tuberculosis and Genius as Manifested in St. Francis of Assisi"

Dr. Oliver T. Osborne (Fellow), New Haven, Conn.:
1 Reprint:
"The Cost of Medical Care"

Dr. Aaron E. Parsonnet (Fellow), Newark, N. J.:
1 Reprint:
"Postinfluenzal Sinus-Nodal Block"

Dr. Virgil E. Simpson (Fellow), Louisville, Ky.:
4 Reprints:
"Diseases of the Cardiovascular System Due to Acquired Syphilis"
"Tularemia"
"Food Content with Relation to Density and Composition of Stone in Upper Urinary Tract" (with Dr. Owsley Grant)
"A Discussion of the Probable Etiological Relationship Between Peptic Ulcer and Vagotonic Syndromes"

OBITUARY

Dr. Archibald Neil Sinclair (Fellow), Honolulu, Hawaii, died October 21, 1930, of heart disease; aged, 59 years.

Dr. Sinclair was born in New York City, but early went to Hawaii where he received his preliminary education at Oahu College. He later attended Glasgow University from which institution he received the degree of Bachelor of Medicine and the degree of Master of Surgery in 1894. During 1916 he did postgraduate study in roentgenology, pathology, bacteriology and blood chemistry at the New York Post Graduate Medical School. From 1901 to 1919, Dr. Sinclair was Assistant Surgeon in the U. S. Public Health Service. At the time of his death, he was Medical Director of The Leahi Home, and bacteriologist of the Board of Health of the Territory of Hawaii.

Dr. Sinclair was a member, ex-secretary and ex-president of the Medical Society of Hawaii; ex-secretary and ex-president of the Territorial Medical Association, ex-secretary of the Honolulu County Medical Society, a member of the American Association of Bacteriologists, a member of the American Association of Immunology, a member of the National Tuberculosis Association, a Fellow of the American Medical Association, and a Fellow of the American College of Physicians. He was elected to Fellowship in the latter organization on February 8, 1921, and had served on its Board of Governors for several years.

Dr. Charles Bowman Bacon (Fellow), Brooklyn, N. Y., died December 10, 1930; aged, 61 years.

Dr. Bacon was born at New Lebanon, N. Y., received his preliminary education at Mount Hermon (Mass.) School and at Cook Academy, Montour Falls, N. Y. He completed two years academic study at Colgate University, and then entered the University of Buffalo School of Medicine, from which he received the degree of Doctor of Medicine in 1897. He interned at Kings County Hospital, 1898-99. From 1905 to 1909, he was visiting physician to the Swedish Hospital; from 1902 to 1909, assistant visiting physician to the Kings County Hospital. Later he was clinical instructor in medicine to seniors from Long Island Medical College. At the time of his demise, he was lecturer in medicine on the staff of the Homeopathic Medical College and Flower Hospital, and medical administrator in the hospital service of the City of New York, Department of Public Welfare.

Dr. Bacon was a member of the New York County Medical Society, New York State Medical Society, the American Medical Association, and had been a Fellow of the American College of Physicians since February 22, 1937.

DR WILLIAM DUFFIELD ROBINSON

Dr. William Duffield Robinson was born at McConnellsburg, Fulton County, Pennsylvania, March 25, 1856. His

ancestry was remotely Scotch-Irish; his parents were John and Mary (Duffield) Robinson. He received his early education in the common schools of his county and later (1872) graduated from the Chambersburg Academy. Coming to Philadelphia he graduated from the Philadelphia College of Pharmacy in 1876. The subject of his thesis was "Tincture Cinchonae Composita". In 1880 he graduated from the Medical Department of the University of Pennsylvania. Dr. Robinson entered upon the practice of medicine in Philadelphia and soon thereafter was appointed Resident Physician to the Eastern Penitentiary, serving faithfully for many years. On October 22, 1891, he married Elizabeth T. Willian, who survives him, together with his four sisters.

In 1914 Dr. Robinson was elected President of the Philadelphia County Medical Society and during his incumbency of that office, appointed not less than eighteen standing committees with definitely assigned duties. These added activities have been and still are advancing and broadening the work and influence of the society, more particularly in the fields of public and preventive medicine.

"At the outbreak of the World War he instituted the Senior Military Medical Association with Dr. W. W. Keen as President. This led to the formation of the Volunteer Medical Service Corps of the United States which was approved by the Council of National Defense in 1918. The object of this Corps was to 'mobilize the medical profession in the present emergency in order to provide for the health needs of the military forces and civil population of the country'. Dr. Robinson was one of the members of the Central Governing Board."[1]

He was an ardent advocate of organized medicine and up to the time of his passing, a regular and interested attendant upon medical society meetings; he felt it incumbent upon himself to become acquainted with the facts and deeper questions involved as far as possible, of practical and scientific medicine. Dr. Robinson possessed a strong civic spirit as shown by his performance of an enormous amount of work in the interests of the public welfare. He was an active member and Treasurer of the Better Homes Committee of Philadelphia; a member and Treasurer of the Committee on Arrangements for Public Health Day in Philadelphia, for many years; he was a member of the Board of Directors of the Pennsylvania Tuberculosis Society, and for a time served as Vice-President, and for many years he served as a member of the Board of Directors of the Oncologic Hospital of Philadelphia. Dr. Robinson also rendered efficient service to his alma mater, the Philadelphia College of Pharmacy and Science, as a member of its Board of Trustees. He was Chairman of the Medical Board of the Sesqui-Centennial International Exhibition.

Dr. Robinson held membership in many local and national medical societies; for example, in the American Medical Association, the Medical Society of the State of Pennsylvania,

[1] WILMER KRUSEN, M.D., in The Weekly Roster and Medical Digest, February 7, 1931.

the Philadelphia County Medical Society (vide ante), the College of Physicians, the Medico-Legal Society, and was an extremely active member of the Philadelphia Psychiatric Society. He also served as President of the American Climatological and Clinical Society, the Philadelphia Medical Club (1924), and the Philadelphia Clinical Society.

Dr. Robinson was Chairman of the General Committee of the National Pasteur Centenary celebration — a magnificent tribute to that true pioneer scientist, the founder of the germ theory of disease. He thus rendered a notable service to the memory of one for whom he had unbounded admiration. He had marked executive ability and it was one of his chief delights to head a committee and lead in planning a celebration in honor of a colleague or some great historic event. He was an interested member of The Sydenham Coterie of Philadelphia—a body of widely known members and specialists of the medical profession holding monthly dinner meetings. For this small group he had "a peculiar affection" and he attended one of its meetings just three days prior to his untimely death.

During committee meetings, which Dr. Robinson faithfully attended, he manifested great resourcefulness in making practical suggestions. His industry was phenomenal; his sympathies were quick and broad; his personality was forceful and ingratiating; his loyalty to friends and his ethical standards were unquestioned, and his bearing was always courteous and dignified. These qualities made him popular and greatly endeared him to his many lay and professional friends. He was a kneen clinical observer and throughout his long professional career followed general medical practice. There is always the risk of unjustifiable asperity in one's judgment of the character of another. It was, however, obvious to those who had an opportunity to trace the developments of Dr. Robinson's character, that he ever sought to achieve what he did not seek for his own sake, but for the good of others—of society. In the death of the subject of this memoir the medical profession has lost a worthy representative; his friends, an agreeable, magnetic, loyal and much beloved comrade. In him the affable, wise physician and sympathetic friend were happily combined.

If space permitted, interesting personal reminiscences revealing Dr. Robinson's capacity for friendship, his versatility and everyday humanity, could be related. Right up to a few days before his passing away, he enjoyed telling stories and relating amusing anecdotes, while time was blotted out for his listeners. It is not too much to say that he radiated good cheer and inspiration to any group in which he found himself, and it is equally true that he gave impetus to the many good causes with which he was identified. It may indeed be said that his indefatigable labors were accompanied with an unusual degree of pleasure, amounting to

"The consummation of all earthly bliss,
The full fruition of a kingly crown."

(Furnished by James M. Anders, M.A.C.P., Philadelphia, Pa.)